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LEUKOCYTIC "INCLUSION BODIES" WITH SPECIAL REFERENCE TO SCARLET FEVER *

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In November, 1911, Döhle¹ described certain "bodies" within the cytoplasm of the polymorphonuclear leukocytes in blood smears from thirty patients with scarlet fever. In a number of controls similar "bodies" were found in a patient with pneumonia and two patients with malignant neoplasms. As far as he knew these "bodies" had not been described before and to them the term "inclusion bodies" (*Leukocytenenschlüsse*) was applied. In March, 1912, Kretschmer² confirmed these findings and considered their presence in scarlet fever of diagnostic value. The latter also found these "bodies" in smears from patients with pneumonia and tuberculosis and two with diphtheria with streptococcus empyema. More recently Nicoll and Williams³ reported a study of fifty-one cases of scarlet fever, finding the "bodies" in forty-five cases. Similar "bodies" were found in three out of twenty-five controls.

The presence of such "bodies" within the polymorphonuclear leukocytes of cases of scarlet fever are mainly of interest from the standpoint of differential diagnosis and of their possible relation to the etiology of this infection. Döhle suspected their relation to streptococcus infections and if these "bodies" are to be found in a large percentage of scarlet fever cases and are absent in non-scarlatinal conditions, they would be of considerable aid in differentiating true scarlet fever from cases of serum sickness with scarlatiniform rashes, *rötheln*, various toxic erythemata, etc.

Accordingly the object of this study was twofold:

1. To investigate the nature of the "bodies."
2. To determine their diagnostic value in scarlet fever after the examination of a large number of cases of scarlet fever, diphtheria, serum sickness and various infections, especially those of streptococcus origin.

*From the Laboratory of the Philadelphia Hospital for Contagious Diseases.

*Read before the Philadelphia Pediatric Society, June 11, 1912.

1. Döhle: *Leukocytenenschlüsse bei Scharlach*. *Centralbl. f. Bakteriol. originale*, 1911, lxi, part ½, p. 63.

2. Kretschmer, M.: *Die Diagnostische Bewertung von Leukocyteneinschlüssen bei Scharlach*. *Berl. klin. Wehnschr.*, March, 1912. No. 11.

3. Nicoll, M., and Williams, A.: *Inclusion Bodies in Scarlet Fever*. *Arch. Pediat.*, 1912, xxiv, No. 5, p. 350.

"INCLUSION BODIES"

These "bodies" are characteristically found in the protoplasm of the polymorphonuclear leukocytes of scarlet fever patients near the margin of the cell and are not connected with the nuclei. They present no fixed morphology but occur characteristically as rod and coccus forms. Due care must be exercised not to mistake the neutrophilic granules for round "inclusion bodies." Both forms may be present in any stage of scarlet fever and in the same smear. Early in scarlet fever most of the polymorphonuclear cells will be found to contain one or more of the "bodies." The number of leukocytes showing their presence and the number of "bodies" per leukocyte vary according to the severity of the infection and diminish as convalescence is established. After the sixth day in mild scarlet fever they may require careful search before being found. The rod or bacillary type is most distinct in outline but all are more or less hazy in the best stained preparations.

TECHNIC

For examination, ordinary blood smears are prepared on perfectly clean slides. Thin smears are especially desirable. The "bodies" are readily stained by the Giemsa, Manson, Leishman, Wright and Jenner stains. Ordinary methylene-blue will bring them out. They do not stain with eosin and hematoxylin. In order to determine whether or not they are composed of chromatin, specific differential stains were employed to differentiate between chromatin and plastin. With the Giemsa stain the "bodies" are colored a faint bluish-green; with methyl-green and pyronin they present a fairly well-defined reddish color and with malachite-green and pyronin likewise a reddish color. They do not stain with iron hematoxylin. These stains would indicate conclusively that the "bodies" do not contain chromatin and are not protozoan in nature. They are probably composed of plastin, represent a degenerative process of the cytoplasm and are probably composed of spongioplasm. The fact that they are found in streptococcus infections would indicate their relation to the streptococcus. However, the systematic examination of the blood of eight rabbits receiving a single injection of streptococci from scarlet fever, puerperal sepsis and tonsils did not show the presence of these "bodies."

SCARLET FEVER

Blood smears from 216 patients with scarlet fever were examined, the majority being cases of mild or moderate severity. A few were of the severe anginose types of scarlet fever. Cases were examined from the first day of the rash to the fifty-second day after the rash had appeared. The results of examination of 200 cases are expressed in Table 1.

It will be noted that "inclusion bodies" are to be found in a large percentage of scarlet fever cases during the first few days of the infection. After the sixth day they become quite few in number and may be more difficult to find. Döhle did not find any after the sixth day but his series

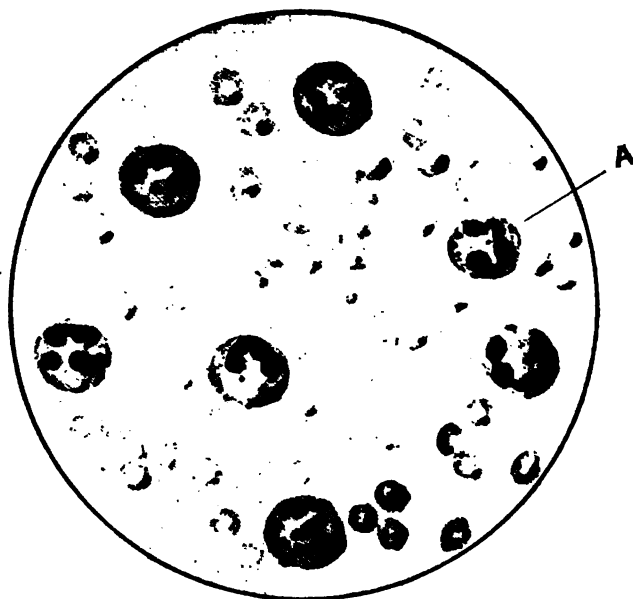


Fig. 1.—“Inclusion Bodies.” Case of scarlet fever. A—neutrophilic granules.

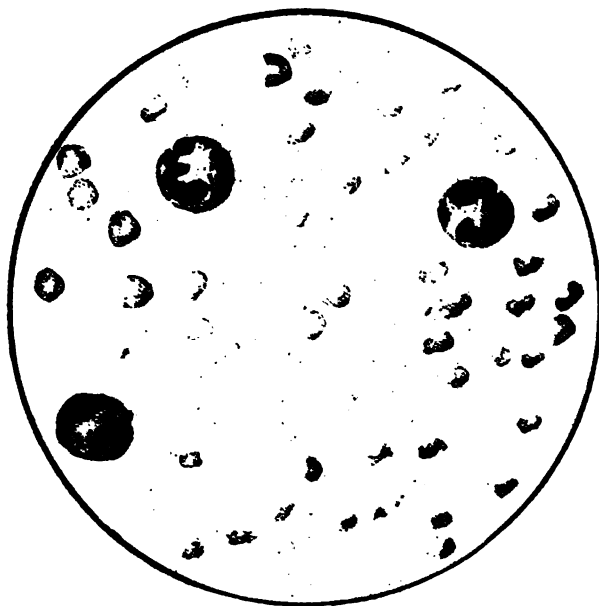


Fig. 2.—“Inclusion Bodies.” Case of scarlet fever following extensive burns of the body.

was rather too small to be conclusive. I found one case, fully convalescent and about ready to be discharged from the hospital, showing typical "bodies" of irregular shape as late as the forty-fourth day. This series includes three cases of scarlet fever following extensive burns of the body, "inclusion bodies" being found in all.

TABLE 1.—RESULTS OF EXAMINATION FOR "INCLUSION BODIES" IN 200 SCARLET FEVER CASES

Day of Disease	Total Examined	Number Positive	Per cent. Positive
First	2	2	100
Second	14	14	100
Third	32	30	93.7
Fourth	14	12	85.7
Fifth	17	12	70.5
Sixth	15	10	66.6
Seventh	13	7	53.8
Eighth	12	3	25.0
Ninth*	9	0	0.0

*From the tenth to fifty-second days, seventy-two cases were examined with positive findings in six cases; one each on the tenth, thirteenth, seventeenth, thirty-sixth, thirty-eighth and forty-fourth days.

DIPHTHERIA

Smears from fifty patients with diphtheria were examined, mainly because the presence or absence of these "bodies" must be determined in this disease if such examinations are to be of value in differentiating serum sickness from scarlet fever. Not a few cases of diphtheria also show the presence of streptococci in the upper air passages along with the diphtheria bacillus.

Table 2 expresses the results.

TABLE 2.—RESULTS OF EXAMINATIONS FOR "INCLUSION BODIES" IN DIPHTHERIA

Day of Disease	Total Examined	Number Positive	Per cent. Positive
Second	4	1	25
Third	10	4	40
Fourth	8	5	62.5
Fifth	8	0	..
Sixth	4	0*	..

*From the sixth to the twenty-first day, 16 were examined, with three positive, all occurring on the seventh day.

It will be noted that these "inclusion bodies" are to be found in a high percentage of diphtheria cases during the first four days of the infection. Therefore if a serum rash should develop within this period the presence or absence of "inclusion bodies" could have no diagnostic importance in differentiating the rash from that of true scarlet fever.

SERUM SICKNESS

Of all the conditions resembling scarlet fever, serum sickness presenting a scarlatiniform rash is most difficult of diagnosis. This is especially true in a hospital for contagious diseases where one must be constantly

on guard to detect scarlet fever and where it is almost impossible to prevent an occasional outbreak in the diphtheria wards. Fortunately most serum rashes are urticarial in nature and easily diagnosed. Scarlatiniform rashes are also prone to develop from the third or fourth to the tenth day after receiving serum and this is a source of further confusion because this period coincides so closely with the usual incubation period of scarlet fever. In my experience the proper diagnosis and management of such cases becomes one of the greatest problems in the hospital management of contagious diseases.

Of thirty cases of serum sickness presenting urticarial rashes, developing, on the average, ten days after admission to the hospital, none showed the presence of "inclusion bodies." Practically all of these cases were examined within twenty-four hours after the appearance of the rash.

I had the opportunity of studying fourteen cases presenting scarlatiniform rashes, thirteen occurring in the diphtheria wards, with the following results:

1. Five were diagnosed clinically as serum sickness and none showed the presence of the "bodies."

2. Five were diagnosed as true cases of scarlet fever and all showed the presence of the "bodies."

3. Two were diagnosed as true scarlet fever but did not show the presence of the "bodies." Both of these cases were very mild in character and developed on the twelfth and thirty-second days, respectively, after admission to the diphtheria wards.

4. One case showed the presence of "bodies" but was of doubtful clinical diagnosis. The child may have had a rash before admission to the hospital but the throat was very much injected and resembled the angina of scarlet fever. The cervical glands were likewise enlarged.

5. Case 14 was that of Dr. C. P. Brown who presented a true scarlatiniform rash over the body but with no other symptoms of scarlet fever. This rash was of gastro-intestinal origin. The leukocytes did not show the presence of "bodies."

MEASLES, ERYSIPELAS, PUERPERAL SEPSIS, ETC.

The blood of seventy-six patients suffering with various infections other than scarlet fever, diphtheria and serum sickness was examined. Most interest centers about those which may be mistaken clinically for scarlet fever and also about those infections due to streptococci.

(a) *Measles*.—Twelve cases, varying from the third to the sixth day after the appearance of the rash, were examined and all were negative. One case was complicated by bronchopneumonia.

(b) *Rötheln*.—But one case was examined, on the second day after the rash made its appearance, and this was negative.

(c) *Erysipelas*.—Eleven cases were examined with positive findings in seven. Of these seven positive cases inclusion "bodies" were found on the third, fourth, fifth, ninth, tenth, twenty-fourth, and twenty-fifth days after the onset of symptoms.

(d) *Puerperal Sepsis*.—One case due to a *Staphylococcus aureus* infection was negative; a second case, infection not determined, showed typical "inclusion bodies."

(e) *Pneumonia*.—Three cases of croupous or lobar pneumonia were examined and in two of these, "bodies" were found. Two cases of bronchopneumonia were negative. Of two cases of empyema, not included in these pneumonia cases, one was positive, and in this case streptococci were found in the pus.

In none of the forty-three additional cases including varicella, pelvic inflammatory disease, pericarditis, goiter, furunculosis, eczema, gonorrhea, mastoiditis, gastro-enteritis, chronic lymphatic and splenomyelogenous leukemia, pernicious anemia, etc., were "inclusion bodies" found.

The presence of these bodies in such a large percentage of cases of erysipelas, in the case of streptococcus empyema and in one of two cases of puerperal sepsis which was likely of streptococcus origin, indicates strongly the relation between these "inclusion bodies" and streptococcus infections.

CONCLUSIONS

1. "Inclusion bodies" are composed of a plastin, probably spongioplastin, and are related to the presence of streptococci.

2. They are present in the polymorphonuclear leukocytes of 94 per cent. of scarlet fever cases during the first three days after the onset of the disease. After this they diminish in frequency and are generally absent after the ninth day.

3. They are to be found in 42 per cent. of diphtheria cases during the first three days of the disease; after this time they are but seldom found.

4. "Inclusion bodies" are found not only in scarlet fever, but in other streptococcus infections.

5. The diagnostic value of these "bodies" is necessarily limited. In serum sickness with a scarlatiniform rash their absence excludes scarlet fever with a fair degree of accuracy. Their presence in this condition, however, may not be due to scarlet fever but to the primary attack of diphtheria. They have, therefore, a negative value.

6. An examination of the blood for these "bodies," however, is very simple and possesses value in aiding a differential diagnosis between scarlet fever, röteln, measles and gastro-intestinal rashes.

I wish to express my thanks to Dr. A. J. Smith, Dr. H. K. Meyers, Dr. S. S. Woody, Dr. E. Laubaugh and Dr. G. Faries for aid in the work.

Second and Luzerne Streets.

THE CLINICAL SIGNIFICANCE OF ABNORMAL RESPIRATION AND DEGLUTITION CLICK OR FREMITUS; THE PNEUMONIC-RESPIRATION-PAUSE-CYCLE

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As respirations normally differ at the different periods of life, so abnormal respiration has a parallel difference as a manifestation of disease in the different periods of life. I may cite, for example, the puerile lung sounds in childhood and adolescence and the diminished and distant respiratory sounds of old age; also the rapid respirations in infantile life and the slower respirations of advanced age; the brief post-expiratory pause in early life and the longer post-expiratory pause in advanced age.

The respirations of exhaustion are in a manner influenced mostly by the age of the patient and partly by the degree of exhaustion.

The breathing of the ill baby or child in exhaustion is shallow, rapid and pauseless, indicating gravity and often impending death. If they fall into slumber while in this condition the respirations lessen in frequency, lengthen in range and are still pauseless. If they awaken unimproved the breathing resumes the characteristics just described; but if, on the contrary, there is an improvement in the patient's condition, the respirations are less rapid, range lengthened, calmer, and an occasional normal post-expiratory pause is noticeable. When in the above clinical picture the disease had merely a remission and a relapse occurs, there is manifested at once a return of rapid and shallow respiration, with no inter-respiratory pause; sometimes this phenomenon precedes the increase of temperature, a natural and usual accompaniment of a recrudescence in disease. When the degree of exhaustion increases, pre-saging death, respiration becomes a little arrhythmical, the inspiratory range being lessened and expiration being more prolonged, this irregularity becoming more accentuated in ratio as the end approaches. The final expiration is well prolonged, with an occasional pause, while a second feeble and aborted inspiration follows, ending in more of an expiratory spasm in which the muscles other than those directly concerned in breathing become involved.

Respirations of middle life in exhaustion differ somewhat from those in earlier life. They are more rhythmical than in infantile life, shallow and rapid, and with no inter-respiratory pause. The ranges of inspiration and expiration are longer and as death approaches the occasional post-expiratory pause is noticeable. The respirations in exhaustion of

advanced age present some peculiarities. Inspiration and expiration follow each other without pause, have a longer range than in earlier life. are irregularly rhythmical, sometimes expiration being longer than inspiration, but soon again rhythm is assumed, and then a rhythm favoring longer expiration. As the exhaustion increases and the patient grows weaker, respirations grow more shallow and a post-expiratory pause is established and prolonged, which continues until death. The latter manifestation is in striking contrast to the post-expiratory pause in infantile exhaustion which is only occasionally apparent and not as continuous as in the last moments of the aged.

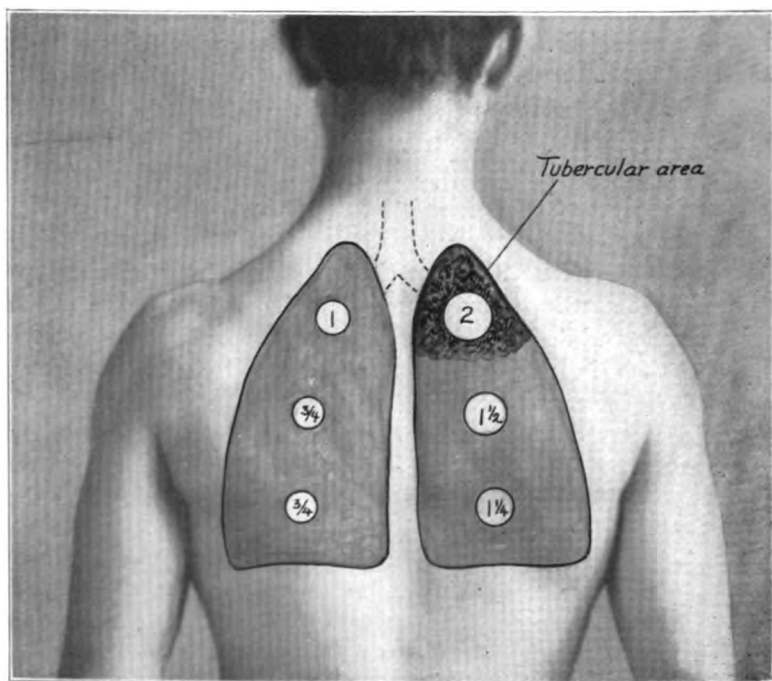


Figure showing by circles posteriorly the different degrees of deglutition fremitus or click in apical tuberculous infiltration of the right lung as compared with the healthy lung.

Respiration of pneumonia in infancy and childhood has a positive and pathognomonic post-inspiratory pause. This pause is not continuous as many suppose. There are usually three to five post-inspiratory pauses, then follows rapid rhythmical respiration without a pause, which ends in one post-expiratory pause and then the post-inspiratory pauses begin again. There is a definite cycle in the recurring post-inspiratory pauses which vary in number from two as a minimum and six as a maximum before the period of rapid pauseless respiration sets in. But the peculiar

point observed is that just at the ending of one phenomenon and before the beginning of the recurrence of the period of the post-inspiratory pause, one prolonged expiratory pause occurs, seeming to link the two changes in some unexplainable physiologic manner. In other words, between the pauseless respirations succeeding the post-inspiratory pauses there appears one prolonged post-expiratory pause, thus leading to the beginning of the cycle. I might name this symptom the pneumonic-respiratory-pause-cycle. It must be remembered that this peculiar respiratory-pause-cycle is generally found in infantile and childhood pneumonia. Infants under 18 months or children 2 years old manifest this condition more strikingly than older children. But let this same pneumonic child fall into sound or natural sleep and all arrhythmia of respiration ceases; then you have still continuing the rapid respirations, but slower than when awake, and absolutely rhythmical and pauseless in occurrence. On reawakening the respiratory-pause-cycle is resumed. Whenever the post-inspiratory pause began to lessen and respiration grew less rapid the pause gradually became more post-expiratory and lessened post-inspiratory. In other words, a transposition of the pause from post-inspiration to post-expiration was a more favorable sign; the lessening of the respiratory pause or its absolute absence coupled with increased rapidity of respiration indicated a tendency to exhaustion and gravity.

I recall a case of bronchopneumonia in an infant 12 months of age with cyanosis, bradycardia and no cardiac murmurs, all indicating a weak heart and the overwhelming severity of the attack. The respirations differed somewhat from the regular type in that inspiration was shorter than expiration. There was the post-inspiratory pause and then a prolonged expiration, pauseless but wheezy like the expiratory wheezing of an attack of bronchial asthma in the adult. Otherwise, the pneumonic-respiratory-pause-cycle was manifested throughout the disease until some hours before death, when rapid and pauseless respiration followed and continued to the end.

Later observations convince me that the pneumonic-respiratory-pause-cycle is nearly always a manifestation of bronchopneumonia, the pneumonia of infantile life, and found in croupous pneumonia when occurring in a child 2 years of age and under. Pneumonia in older children presents less of the respiratory pause-cycle, but one finds a more continued and more pauseless respiration and the altered pulse-respiration ratio is more marked than in earlier life. I have sometimes found a pleuritic complication attended with pain in inspiration productive of irregular pauses in respiration, evidently a suspension of breathing to alleviate pain.

My experience leads me to believe that in cases of children of lowered vitality from disease other than lung troubles, manifesting cerebral symptoms, regularity of respirations negatives organic brain disease. This rule can also be applied to the pulse.

If an infant having apical pneumonia with the characteristic respirations develops cephalic symptoms, and the breathing does not change from the pneumonic-respiratory-pause-cycle, one may conclude that the brain symptoms are merely symptomatic and not organic in character. The absence of persistent vomiting is confirmatory of this conclusion.

Parenthetically, I have observed another point while closely studying the respirations of pneumonic children:

If one places the hand on the right and left flanks of the sick child one will notice a greater sinking of the side having the pneumonic lung. This observation I have frequently verified.

In the respiration of pneumonia of adults the normal respiratory pause is entirely missing, inspiration and expiration following each other in close succession. As exhaustion increases respiration grows more rapid, shallow and somewhat labored. The moment the crisis begins there is a return of an occasional post-expiratory pause and less rapid breathing.

In the early convalescence of adult pneumonia during sleep respiration becomes slower and the normal post-expiratory pause is continuous; even when during the preceding waking there is not a continuous post-expiratory pause, with some accelerated pauseless breathing.

In a case of adult pneumonia from which the above observations were made I noticed the following: One-half to one minute before awaking respirations became pauseless and rapid and remained so until semi-consciousness merged into full consciousness when approximately normal breathing followed. This manifestation is probably more physiologic than pathologic.

In the extremely aged there is a form of respiration accompanying bronchial catarrh in which there is shallow and accelerated breathing, with only an intermitting post-expiratory pause, with moist and dry râles, indicating presumably a pulmonary edema, the other symptoms not being in accord. I ascribed this condition to an associated nervous element and it is seemingly more dangerous than real. The same clinical picture in a young adult would portend greater evil.

By the term deglutition fremitus I mean the sounds occasioned by the act of swallowing which are more readily conveyed to the ear through the area of a pneumonic induration. In the adult it does not seem as valuable as the transmitted voice, but in infantile pneumonia, where the act of crying is the sole manner of expression, this diffuses itself throughout the lungs in such a way as to confuse. Let the suckling infant nurse and while the ear is auscultating the lungs posteriorly note the area conveying the noise of the act of swallowing. A gurgling or clicking sound heard more distinctly at any point will indicate a pneumonic spot. Repeatedly I have verified this observation but it requires tact, time and patience to derive the benefit from this aid to the diagnosis of pneumonia.

While other well-known symptoms are more positive diagnostically, a decided aid in localizing indurated areas may be obtained by deglutition fremitus. Could we but request the infant to modulate the sound of crying or soften the voice we would have an equally valuable aid in the diagnosis of lung consolidation as in adult vocal fremitus, but this is impossible.

The examination should be made after the infant has fasted for a long time and then when put to the breast it nurses with a feverish thirst and hunger and consequently swallows oftener and greater quantities, which aids in accentuating the deglutition fremitus through indurated area.

I am justified in calling deglutition fremitus, deglutition click, the pronunciation of the latter word "click" corresponding to the fremescent sound heard when auscultating the chest during the act of swallowing. The following peculiarity developed in the course of my examination: Over a left apical tuberculous indurated area posteriorly the deglutition click or fremitus was decidedly distinct, and as I passed down to the middle of the lung over a non-indurated area the fremitus was slightly lessened. Over the base of the apically indurated lung, or over the normal lung tissue, the fremitus was still accentuated but less distinct than that of the middle area and the latter fremitus was less distinct than that of the apical area.

Examining the healthy lung of the same individual, deglutition fremitus was alike in pitch and tone over the entire lung, possibly a little more accentuated at the apex. But the three distinct degrees of deglutition fremitus of the healthy lung were measurably less than over any area of the apically diseased lung.

In the accompanying illustration I can better explain the difference in intensity of sounds as evidenced over the lung area of one lung partly diseased and the lessened deglutition fremitus of its non-diseased fellow.

Let an imaginary circle 2 inches in diameter be drawn over the indurated lung area posteriorly and one circle $1\frac{1}{2}$ inches in diameter over the middle non-indurated lung area of the same lung, and a third circle $1\frac{1}{4}$ inches in diameter over the base of the same lung. Then draw a circle of 1 inch over the apex posteriorly to the opposite healthy lung, and two circles of three-fourths inch in diameter over the middle and basilar area of the same lung. You will now have a guide as to the variety of fremitus produced by the act of deglutition. The 2-inch circle represents the maximum of intensity over the tuberculous, infiltrated apex and the three-fourths-inch circle represents the base of the opposite healthy lung — the most remote area from the diseased tissue — giving the less distinct deglutition click or fremitus; the three-fourths-inch circle

representing a minimum as compared with the 2-inch circle over the tuberculous area as a maximum of fremitus.

My studies and observations in deglutition fremitus or deglutition click are yet embryonic and this paper merely embodies a preliminary report. I do not believe the developments thus far contribute much in the way of a decided and valuable aid to diagnosis, but my purpose is to call the attention of the profession to a hitherto neglected element in physical diagnosis which can be further evolved on a practical basis by the great body of medical practitioners, who are the final arbiters of all the novelties in medicine and diagnosis. They must affirm or reject a proposition on its merits. The child cannot be asked to say one, two and three, or be requested to alter its respiration like an adult, but the act of swallowing is instinctive and automatic and can be readily produced even in a new-born infant.

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THE RELATIONSHIP BETWEEN THE INFECTION IN THE CHILD AND CLINICAL TUBERCU- LOSIS IN THE ADULT *

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Most painstaking inquiry into the clinical history of patients suffering from clinical tuberculosis fails, in nearly all instances, to reveal with any degree of certainty the time when the infection occurred. Especially is this true in adults, for tuberculosis is not the disease that we have long thought it to be. The time of infection and the time when clinical symptoms manifest themselves is, as a rule, most probably separated by years. We must not expect an exposure to infection and an immediate manifestation of symptoms. It is just as important, in fact, more important, to know that the patient associated intimately with some one suffering from tuberculosis when a child, as to find an exposure immediately prior to the manifestation of symptoms. Some German authors,^{1, 2, 3} are considering tuberculosis as a disease of three stages, the same as syphilis; first, that of the infection of the regional lymph-nodes; second, the stage when the disease spreads to new areas, and third, the late manifestations.

The cutaneous tuberculin test as given us by von Pirquet has done more to help us understand the nature of tuberculosis than any other means.

Hamburger⁴ says he agrees with those observers who believe that if a child develops tuberculosis within the first two years of life a careful examination into the clinical history will determine the source of infection in the majority of cases. This can well be done during the first two years of life, for during this period tuberculous infection is comparatively rare, and when it does come it usually manifests itself in one of the rapid

*Read in the Section on Diseases of Children of the American Medical Association at the Sixty-Third Annual Session, held at Atlantic City, June, 1912.

1. Ranke: Vortrag in der Gesellschaft für Kinderheilkunde. München. med. Wehnschr. No. 15, April 12, 1910, p. 826; Ueber den zyklischen Verlauf der menschlichen Tuberkulose, Brauer's Beitr. z. Tuberkulose, 1911, xxi, Part 1.

2. Von Pirquet: Vortrag von dem Deutschen Zentral Committee zur Bekämpfung der Tuberkulose, Berlin, June, 1911. Cited by Ranke.

3. Hamburger: Ueber Spätformen der Tuberkulose. München. med. Wehnschr., March 19, 1912.

4. Hamburger: Allgemeine, Pathologie u. Diagnostik des Kindertuberkulose, 1910. Die Tuberkulose als Kinderkrankheit. München. med. Wehnschr., No. 25. 1908, No. 25.

forms, developing soon after the inoculation and showing threatening symptoms as quickly as the disease can develop; and usually proving rapidly fatal. There is almost no tendency to chronicity in the disease as it manifests itself in these very young children. As the child becomes older, however, the disease assumes more of a chronic course, which is another way of saying that the child has begun to manifest a degree of immunity toward the tubercle bacillus.

This fact is easily explained according to the modern theories of immunity and the explanation is borne out by experimental evidence. Individuals suffering from tuberculosis are found everywhere and many of them do not know that they have the disease until long after it becomes an open lesion. The consequence of this is that bacillus-bearing sputum is scattered carelessly here and there, wherever human beings dwell. Tuberculous cattle are also found in nearly all of the dairy herds, thus infecting quite a large amount of the milk which is consumed. The child begins his first fight with the bacillus, then, as soon as he begins to come in contact with people and take food produced otherwise than by his mother's breast; and particularly when he reaches the age of playing on the floor, for it is a well-established fact that tubercle bacilli are thickest on the floor and near the floor. They are carried into the home in one way or another and remain viable for long periods of time. This is also the time when the child begins to eat food, the production and preparation of which are difficult to control, and the time when the child begins to associate with other children.

The question of infection is a question of dosage of bacilli. If the child takes in only a few bacilli at first, they stimulate the child's cells, antibodies are produced and the invading bacilli are destroyed with a resultant increase in the child's antibodies, or, in other words, a heightened immunity or resistance is established against further infection with tubercle bacilli. The child is now fortified against a larger dose of bacilli than before. This same thing, inoculation followed by destruction of the bacilli, is repeated time after time until quite a degree of immunity is gradually established; but not enough, however, in most instances, to protect the child from an infection occurring, as is shown by the fact that nearly all children are infected with tubercle bacilli before the fifteenth year is reached, according to the statistics of Hamburger, von Pirquet, Gangenhofner and others. Nearly every child comes in contact with more bacilli than he can overcome sometime before he reaches the age of puberty. That all of these children do not develop clinical tuberculosis is well known; so the inquiry "What becomes of these infections?" is pertinent. A small percentage develop acute tuberculosis and die quickly; another comparatively small percentage develop a chronic tuberculosis; another group shows no definitely recognizable symptoms that

have been heretofore considered as due to tuberculosis, but suffers from the infection and fails to develop a natural physical strength; while the great majority remain free from symptoms and develop in a normal manner, as far as we are able to tell. The chances of the child showing acute symptoms diminishes with age, there being comparatively less acute tuberculosis after the fourth year, as shown in Tables 1, 2 and 3.

The after-history of these last two classes shows the development of quite a large percentage of our clinical tuberculosis; and it is the explanation of the clinical disease and its relation to the early infection that I now wish to consider.

CLINICAL TUBERCULOSIS AND EARLY INFECTION

The evidence adduced from animal experiment is very important and convincing. The presence of a tuberculous focus, either healed or unhealed, affords a certain though variable degree of immunity to the animal harboring it. The writer elaborated this point quite fully in a paper read before the Medical Society of Greater New York, March, 1910,⁵ and will quote from it.

"For some time it has appeared to me that patients suffering from tuberculosis must develop a certain degree of immunity to the bacilli producing their own infection at least; otherwise they would have no chance for life against the countless myriads of bacilli which are thrown into their air passages and which are swallowed by them daily during the period of a long illness. But in spite of this opportunity for inoculation, which is present even for years in many instances, patients recover. If the number of bacilli which are found more or less constantly in the air passages of patients with open tuberculosis of a moderately advanced degree were placed in the air passages of healthy individuals, or, if the number swallowed by such patients were injected into the alimentary canals of healthy individuals, we certainly would expect infection to occur.

"Recent experiments of Calmette,⁶ Hamburger,⁷ Römer⁸ and others show that through the first infection an immunity is developed, which affords protection against further infection from both the bacilli within the body and from those coming from outside sources. Guinea-pigs, rabbits, sheep and cattle which have been once infected with tuberculosis show a resistance to a second infection that can only be accounted for by the presence of a considerable degree of immunity.

"It is self-evident that the greater the degree of immunity present the more chronic the disease. This is noted in the manner in which tuberculosis destroys people who have not been previously inoculated with the disease, such as the Africans and people of the Faroe Islands, as compared with the way it affects the inhabitants of Europe and America. It is also noted in children in the early months of life when compared with children in later years. During the first year

5. Pottenger: Immunity in Tuberculosis Considered from Both the Experimental and Clinical Standpoints. *Med. Rec.*, New York, June 18, 1910.

6. Calmette: Nouvelle contribution à la étude de la Vaccination des bovidés contre la Tuberculose. *Ann. de l'Inst. Pasteur*, September, 1908.

7. Hamburger: Die pathologische Bedeutung der Tuberkulin Reaction. *Wien. klin. Wchnschr.*, 1908, No. 29.

8. Römer: Weitere Versuche über Immunität gegen Tuberkulose durch Tuberkulose zugleich ein Beitrag zur Phthiseogenese. *Beitr. z. Klin. der Tuberkulose*, 1909, xi, and xiii.

of life tuberculosis is nearly always acute, assuming the meningeal or acute miliary form. Hamburger¹ gives the following interesting statistics of tuberculosis in childhood as presented by post mortem evidence at the St. Ann Kinder-spital, Vienna, from 1903 to 1906, inclusive.

TABLE 1.—MORTALITY OF TUBERCULOSIS BY AGE PERIODS

Periods	From Birth to 3 mos.	4-6 mos.	7-12 mos.	Total	2 years	3-4 years	5-6 years	7-10 years	11-14 years
Number of cases...	4	13	32	49	74	102	38	41	31
Fatal cases	4	13	27	44	51	69	23	28	16
Per cent. of fatality	100	100	80	90	70	67	60	68	50

TABLE 2.—FREQUENCY OF HEALED TUBERCULOSIS BY AGE PERIODS

	1 year	2 years	3-4 years	5-6 years	7-10 years	11-14 years
Total number of cases	49	74	102	38	41	31
Number with signs of healing..	0	0	7	4	7	10
Per cent. of healed tuberculosis .	0	0	7	10	17	33

"He also cites the following table (Table 3) from Hamburger and Sulka:

TABLE 3.—RELATIVE FREQUENCY OF ACUTE AND CHRONIC TUBERCULOSIS BY AGE PERIODS

	1 year	2 years	3-4 years	5-6 years	7-10 years	11-14 years
Miliary or meningeal tuberculosis	13	19	28	10	8	2
Chronic general or pulmonary tuberculosis.....	7	6	6	1	4	6
Total fatal cases	20	25	34	11	12	8

"These statistics show that tuberculosis is nearly always fatal in the first years of life; in 90 per cent. the first year, 70 per cent. the second, with a gradual decrease so that by the time puberty is reached the mortality has fallen to 50 per cent. Another interesting fact is found in Table 2. No tendency to healing is manifested during the first and second years and only in 7 per cent. in the third year. By the time puberty is reached signs of healing appear in 33 per cent. Table 3 shows that of twenty cases in the first year of life, thirteen were cases of acute miliary or meningeal tuberculosis; of twenty-five cases in the second year nineteen were acute miliary or meningeal tuberculosis, and of thirty-four in the third year, twenty-eight were of this form, while between the eleventh and fourteenth years of eight cases only two were of these acute forms."

The facts adduced by these clinical observations and experimental results warrant the assertion that an individual who has a tuberculous lesion already present in the body develops a marked protection against further inoculation with bacilli, and that if a further extension of the disease is to occur from the focus already within the body, or a new infection is to occur from without, it must be by an inoculation of sufficient bacilli to overcome the increased protection which is present as a result of the previous infection. For conclusive proof of this point I would refer to the experiments detailed by Römer in his most valuable report.⁶

That such an inoculation occurs now and then in adult life we can readily believe, especially in such instances as where a husband develops the disease after a wife, or vice versa, when sufficient precautions have not been taken; or when a brother or sister follows another brother or sister. Even in these cases, however, we are not sure that the infection comes from without. In many such cases that I have examined I have felt that it was just as probable that the disease in the second member was from an old focus from within and that the cause of the lesion was an extension resulting from the lowered resistance caused by the reduced physical and depressed mental condition of the patient.

The usual clinical history of patients suffering from tuberculosis when carefully analyzed leaves little doubt that the disease as it presents itself is either a new activity in, or an extension from, an old focus. In those cases in which the first symptom is hemoptysis, or those coming on, following some illness such as influenza, bronchitis or pneumonia, or those in which it comes on suddenly with cough, fever and expectoration, there is little doubt that the acute symptoms are a manifestation of activity in an old focus. In those cases in which the illness comes on slowly, with feelings of indisposition, slight digestive disturbances, a gradually developing cough, the question is a little more difficult to decide; but careful consideration will place most of these in the same class. It is impossible to obtain a history in more than a minor portion of our tuberculous cases wherein we could feel at all certain that the given infection was due to a definite exposure to bacilli.

PREVENTION

The preponderance of clinical evidence, then, throws our clinical tuberculosis, as it manifests itself in adult life, back to those early infections which occur in childhood. It is essential to understand this relationship because of its bearing on the rational measures to be adopted for its prevention and cure.

It is these early infections which occur in childhood that eventually cause the clinical tuberculosis in adults, and which are responsible for the enormous mortality from this disease; then, the stamping out of tuberculosis, if it is ever attained, must come through either preventing the

infection from occurring, holding it in a state of quiescence, or healing it out when it has once occurred. It seems almost an impossibility to think of being able to control the large majority of cases of open tuberculosis, which would be necessary in order to stamp out the disease by taking away the danger of infection. This difficulty is greatly increased by the fact that the open stage is often reached months and even years before the diagnosis is made. While we must surround the open cases with the most approved hygienic measures so as to take away every possible source of infection, yet I cannot believe that such measures alone will ever stamp out tuberculosis. It must be stamped out by making the individual immune to infection or by curing the infection when it has occurred, thus preventing it from reaching the open stage.

Personally, I believe that the prevention of tuberculosis will come through vaccination; and, if I interpret the works of our leaders rightly, such a desideratum is not as far off as many believe. The experimental studies on immunity made by such men as Koch, Behring, Maragliano, Wright, Römer, Wolff-Eisner, Calmette, Spengler, Trudeau, von Ruck, and others, and the very interesting reports by the use of the living bacillus, made by Webb, are blazing the way for one of the greatest boons to the human race, the production of a positive immunity.

We, as physicians, however, cannot wait for this to come about, but we must continue attacking the problem in every way that offers a partial solution. We must continue our educational measures, especially instructing those afflicted with the disease in the methods of preventing its spread. Remembering the great percentage of the human family that harbors foci of infection, we must push the campaign for more hygienic living, thus hoping to prevent quiescent lesions from taking on activity. We must endeavor to cure as many patients suffering from clinical symptoms as possible.

But, what of these children who are infected? Should we disregard them as we have in the past and wait for them to become clinically tuberculous before offering them help? Of course we realize that while it is possible that at least 75 per cent. of all children are infected before they reach the fifteenth year, probably not more than 20 per cent. will develop what we are able to diagnose as clinical tuberculosis, and not more than 10 or 15 per cent. will die of the disease. This means that the children have three chances out of four of never knowing that they have an infection if left alone, and that they have about six chances out of seven of not dying of the disease. The question for us to settle is this: Is the percentage of morbidity and mortality, when compared with the total number of infections, sufficient to warrant the medical profession in attempting to heal out all the infections which can be determined in childhood? The recognized rule in syphilis is to heal out all those who show

a positive Wassermann. The best thought in medicine and surgery is to make early diagnoses and apply measures for the eradication of disease as early as possible; and, as a result, deaths from such diseases as diphtheria, appendicitis and gall-bladder infections are becoming rare. Shall we treat tuberculosis the same? If so, then it is the province of the pediatricist to control clinical tuberculosis. We have the various tuberculin tests at our command. They can be given with ease and without fear of harm. They are specific in their action. If the operator will learn the few conditions under which they may sometimes fail to react, even though an infection be present, he will have at his command a most reliable diagnostic method. Conditions which cause the tuberculin reactions to remain in abeyance, even though infection be present, are as follows: an advanced tuberculosis, a cachectic condition, a very low state of nutrition and the presence of some of the acute infectious diseases, notably measles. When these conditions are present a negative reaction does not signify that tuberculosis is not present.

If it is right to treat every patient for syphilis if he reacts to the Wassermann test, is it not equally just to afford the patient reacting to tuberculin the same protection? Is not the comparative greater seriousness of the disease an argument for such a course?

I believe that it is the physician's duty to seek out these children who are infected and put them on a hygienic regimen which will favor a natural physical development. Those in whom the disease shows signs of activity should be treated with tuberculin as well as with the usual hygienic dietetic measures; for we now have sufficient clinical data to show beyond doubt that a greater percentage of patients treated with hygienic and dietetic measures, plus tuberculin, heal out than where the disease is treated with hygienic measures alone. It might further be stated as an additional reason for treating infected children that they respond better to treatment than adults do.

RECENT ADVANCES IN OUR KNOWLEDGE OF MEASLES

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While it has been quite the general belief for years that the infection of measles is contained in the blood and in the nasal and buccal secretions and, perhaps, in the "scales," it is surprising on what inconclusive data this belief has been based.

Previous to 1905 the data as to the infectivity of the blood, while highly suggestive, were by no means conclusive; but in that year Hektoen reported the infection of two men with measles by inoculation with an ascitic broth culture of blood drawn from human cases of the disease during the first thirty hours of the eruption. These results left no doubt as to the presence of the virus of measles in the blood during at least the first thirty hours of the eruptive period.

The state of our knowledge as to the presence of the virus in the nasal and buccal secretions was even more unsatisfactory than that in regard to the blood, although clinical observations and Mayr's experiments on children had made it fairly certain that these secretions were infective for man, and the same author's negative experiments with the "scales" had also shown that it was fairly certain that these did not contain the virus of the disease.

The literature of measles contains many reports of attempts to produce measles by various procedures in animals other than monkeys, but Josias¹ seems to have been the first to attempt to inoculate the monkey with measles. His work had been inspired by Chavigny's² reported observation of a monkey that had developed measles after having been in close contact with a case of the disease in the person of its keeper. In 1898 Josias reported attempts to infect monkeys with measles by various methods and he apparently obtained positive results in some instances.

1. Josias, Albert: *Recherches expérimentale sur la transmissibilité de la rougeole aux animaux*. Med. moderne, Paris, 1898, ix, p. 153.

Mayr, Frantz: *Beobachtungen über Masern*, etc. Zeitschr. d. k. k. Gesellsch. d. Aerzte zu Wien, 1852, i, 13; *Masern*. Virchow's Handb. der special Path. u. Therap., 1860, iii, Part 3, p. 106.

2. Chavigny, Paul: *Un cas de rougeole chez un singe*. Bull. méd. Paris, 1898, xii, p. 334.

Grunbaum³ in 1904 reported attempts to infect two chimpanzees by various means, including the injection of blood drawn from the median basilic vein of patients with measles, but he regarded his results as negative.

On account of the prominent place occupied by measles in our morbidity and mortality statistics, it appeared to us highly important that studies be made on the disease to determine its cause, means of transmission and prevention. In view of the apparent insusceptibility of the lower animals to measles it seemed to us most desirable that the susceptibility of the monkey to the disease be thoroughly tried out.

AUTHORS' EXPERIMENTAL WORK

In pursuance of this plan we began our work⁴ on experimental measles early in the summer of 1910 by inoculating two rhesus monkeys with blood from a patient with measles. In each of the animals a slight rise in temperature, eleven days after inoculation, was noted, but an interpretation of its significance was not possible.

With blood from our second patient we also inoculated two monkeys with a result similar to our first case. With blood from our third patient we inoculated three monkeys. Ten days after inoculation there was noted a slight rise in the temperature of one of the animals. At the same time there appeared a few papules on the face, brows and chin with a diffuse erythema of the brows and eyelids. The rise in temperature was not sustained. At the end of four days the eruption had perceptibly faded, and a fine branny scaling was noted at the site of the fading papules. This result we were inclined to consider as indicating a mild attack of measles, even though an attempt at passage with blood drawn soon after the eruption was first noted, resulted negatively.

The thought was constantly present in our minds from the beginning of our work with measles that we should obtain blood for inoculation as early in the disease as possible, and fortunately we saw our fourth patient at not less than fourteen hours after the eruption first appeared. With blood drawn from this patient about fourteen hours after the eruption was

3. Grunbaum, A. S.: Some experiments on enterica, scarlet fever, and measles in the chimpanzee; a preliminary communication. *Brit. Med. Jour.*, April 9, 1904, p. 817.

4. Anderson, John F., and Goldberger, Joseph: Experimental Measles in the Monkey: A Preliminary Note. *Pub. Health Rep.*, June 9, 1911, p. 847; Experimental Measles in the Monkey: A Supplemental Note. *Pub. Health Rep.*, June 16, 1911; The Period of Infectivity of the Blood in Measles. *Jour. Am. Med. Assn.*, July 8, 1911, p. 113; Goldberger, Joseph, and Anderson, John F.: An Experimental Demonstration of the Presence of the Virus of Measles in the Mixed Buccal and Nasal Secretions. *Jour. Am. Med. Assn.*, August 5, 1911, p. 476; The Nature of the Virus of Measles. *Jour. Am. Med. Assn.*, Sept. 16, 1911, p. 972; Anderson, John F., and Goldberger, Joseph: The Infectivity of the Secretions and the Desquamating Scales of Measles. *Jour. Am. Med. Assn.*, Nov. 11, 1911, p. 1612.

first noted, and before the temperature had reached its maximum, we inoculated two rhesus monkeys. Ten days after inoculation the temperature of both animals showed a distinct rise and both developed an eruption. Blood drawn from the hearts of both of these monkeys was used for the inoculation of other monkeys, some of which developed febrile reactions and eruptions. This strain of measles virus was successfully propagated by blood inoculations through six monkey generations, when it was discontinued. The results obtained from the inoculations made from our fourth patient plainly showed us that the monkey was susceptible to measles by blood inoculations, but that this susceptibility was not acute and apparently was subject to quite considerable individual variation.

Since our work was reported three papers by different workers have appeared corroborating our results as to the susceptibility of the monkey to measles. Hektoen and Eggers,⁵ while mainly occupied in their work on experimental measles in the monkey with a study of the leukocytes, state that the general results of their experiments agree very well with those reported by Anderson and Goldberger.

Nicolle and Conseil⁶ reported the infection of the bonnet monkey with measles by the inoculation of blood drawn twenty-four hours before the first appearance of the eruption, and in a recent paper Lucas and Prizer also confirm our work as to the susceptibility of the monkey to measles by blood inoculation, and are the first to report the observation of Koplik spots in the monkey.

LIMITATION OF INFECTIVITY

The results obtained by these workers emphasize the statement made by us in our second paper⁴ as to the variation in susceptibility of monkeys to measles, but the variability in susceptibility of the animals to the disease while apparent early in our work, did not, in our opinion, fully explain the uncertain results obtained from the inoculations made from our first three patients. For that reason, after we had obtained such striking results from the inoculations made from the fourth patient, we carefully went over the notes of our first three cases to determine if possible whether this question of the susceptibility of the monkey was the only factor, or if there was not some other factor having something to do with the inconclusive results from our first three cases.

5. Hektoen, Ludvig, and Eggers, H. E.: *Experimental Measles in the Monkey with Special Reference to the Leukocytes*. Jour. Am. Med. Assn., Dec. 2, 1911, p. 1833.

6. Nicolle, Ch., and Conseil, E.: *Reproduction expérimentale de la rougeole chez le bonnet chinois. Virulence du sang des malades 24 heures avant le début de la éruption*. C. R. de Acad. Sci., Dec. 26, 1911, cliii.

We found that the blood from our first three patients had been drawn after intervals of at least twenty-four to forty-two hours after the first appearance of the eruption, whereas the blood from our fourth patient had been drawn at the end of not less than fourteen hours after the eruption first appeared. The thought at once occurred to us that in measles we might have a disease in which the infectivity of the blood was more or less limited to the early period of the disease, as is the case, for example, in yellow fever, and that this limitation of infectivity of the blood was one of the factors concerned in the inconclusive outcome of our first three experiments.

In order to test this hypothesis, we drew blood from a patient with measles about six hours before the eruption first appeared. The patient was again bled exactly twenty-four hours later, or about eighteen hours after the first appearance of the eruption; the third bleeding was forty-five hours after the second, and the fourth forty-eight hours after the third. At least two monkeys were inoculated from each bleeding as soon thereafter as possible. Both of the animals inoculated with blood drawn before the eruption appeared, gave a definite febrile reaction but no eruption; all three of the animals inoculated with the blood (one with serum, one with washed corpuscles, and one with defibrinated blood plus normal monkey blood) drawn eighteen hours after the first appearance of the eruption, gave well-marked reactions, including the presence of an eruption and involvement of the respiratory apparatus; no evidence of a reaction in one and at most a very doubtful reaction in the second of the two animals inoculated with blood drawn sixty-five hours after the eruption first began to appear; no indication of a reaction in either of the two monkeys inoculated with blood drawn 113 hours after the first appearance of the eruption.

These results taken with those reported by other observers since our work first appeared, point strongly to a period of infectivity of the blood beginning at least twenty-four hours before and continuing for about twenty-four hours after the first appearance of the exanthem. At the end of twenty-four hours from the first appearance of the eruption the infectivity of the blood for the rhesus monkey appears to be greatly lessened and becomes progressively less thereafter.

The existence of a more or less definitely limited period of infectivity of the blood in measles and the variation in susceptibility of the monkey to the disease would explain both the negative and positive results of Josias, would throw light on the inconclusive results of some of our earlier experiments and the reported failure of other workers, and make understandable the opinion almost universally held heretofore that the monkey is not susceptible to measles.

NATURE OF THE REACTION IN MONKEYS

Before entering on a discussion of other results of our work with measles it would seem to be advisable to discuss briefly the nature of the reaction of the monkey to the disease. It has been shown that at least three species of the lower monkeys, *Macacus rhesus*, *Macacus cynomolgus*, and *Macacus sinicus*, are susceptible to measles, and it is quite probable that all monkeys are capable of taking the disease. Monkeys may be infected by introducing the virus into the body by any one of the usual methods of inoculation; but we have used, by preference, the intravenous method in most of our work. They also may contract the disease when placed in a cage with a sick monkey during, at least, the early period of the disease. When infection is produced by inoculation, the incubation period may be as short as five days or exceptionally as long as twenty-two days; but the average may be said to be approximately six to eight days.

The first indication of a reaction is usually a rise in temperature, especially a rise in the morning, with a sustained or higher reading in the afternoon; the temperature may remain at about the same level for four or five days and then drop rather sharply and remain down, unless there is a complicating bronchitis or pneumonia. The eruption usually begins to appear on about the third day after the rise in temperature begins, though it sometimes is coincident, or may be as late as the fourth or fifth day. In most cases it is first noticed on the chest or abdomen and may spread to the thighs, arms, and face. On account of the thick fur and dark skin the eruption is not so plainly discernible on the other portions of the body. It sometimes happens that the eruption begins to fade where it first appeared, while still appearing on other parts. As the eruption fades it may be followed by a fine branny desquamation. There is more or less variation, just as there is with human measles, in the appearance of the eruption; but the typical rash first appears as minute red spots which not infrequently coalesce, forming large patches; they soon begin to fade, but a stained spot may persist for several days. The eruption is not invariably present, but blood from monkeys with a distinct febrile reaction and with or without the respiratory symptoms has been found infectious. There is frequently coryza and coughing. In some instances the animal has been killed and found to have had a bronchopneumonia or even a lobar pneumonia. Some of our animals have presented as typical a picture of measles as will be seen in a well-marked case of the disease in human beings. Koplik spots have been observed by Lucas and Prizer.⁷

A monkey that has had a definite reaction is found to be immune to a subsequent inoculation with virulent blood.

7. Lucas, W. P., and Prizer, E. L.: An Experimental Study of Measles in Monkeys. Jour. Med. Research, April, 1912.

NATURE OF THE VIRUS

As before stated, the susceptibility of the rhesus monkey to measles appears to be subject to considerable variation, for it has not infrequently been found that when two animals were inoculated with the same material only one developed the disease, or that one gave a more marked reaction than the other.

As soon as we had definitely determined that the monkey was susceptible to measles by blood inoculation, we gave our attention to a study of the nature of the virus as it exists in the blood, and for this purpose made experiments to determine its filterability, resistance to drying, to heat, to freezing, and to age.

We found that the virus in measles blood is capable of passing through a Berkefeld filter, that it may resist desiccation for twenty-five and one-half hours, that its infectivity was destroyed by heating at 55 C., for fifteen minutes, that it resisted freezing for twenty-five hours, and possibly retained some infectivity after keeping twenty-four hours at 15 C.

NASAL AND BUCCAL SECRETIONS

In order to test the infectivity of the nasal and buccal secretions from human cases of measles, we obtained such secretions from a patient with the disease and made serial inoculations with these secretions at different stages of the illness. We found that the secretions from this case were infective for the monkey at the time of the first appearance of the eruption, and again forty-eight hours later; that is, early in the fourth day and early in the sixth day of the disease, and that this infectivity was due to a living virus susceptible of transfer from monkey to monkey by blood inoculation.

In order to determine the duration of the infectivity of the secretions, we made inoculations in monkeys with the secretions collected at various periods of the disease from five additional patients.

Without going into the details of these experiments it is sufficient for the purposes of this paper to say that, viewing our experiments with secretions as a whole, it would appear that the nasal and buccal secretions in uncomplicated cases of measles may be at times, but are not always, infective for the monkey, and that the positive results were obtained only with secretions collected in the twenty-four- and forty-eight-hour period of the eruption.

Our experiments so far do not permit us to draw definite conclusions as to the duration of the infectivity of the secretions, but we believe that our results tend strongly to suggest a reduction, if not a total loss, of infectivity of the nasal and buccal secretions with the approach of convalescence.

INFECTIVITY OF THE "SCALE"

We made three experiments⁴ to determine the infectivity of the measles "scales" collected from human cases of the disease from four to seven days after the first appearance of the eruption. In not a single one of the monkeys — two in each experiment, or six altogether — was there the least evidence of a reaction. Alone, the negative results of these experiments, while highly suggestive, would hardly justify the conclusion that the desquamating epidermis is not infective for man; but, when viewed in the light of Mayr's negative results in children, we believe that the desquamating epithelium in measles does not, in itself, carry the virus of the disease.

CULTURES

We have made many cultures with measles blood known to be infective by monkey inoculations, but in no instance have we been able to obtain a growth that appears to have any etiologic relation to the disease.

THE DIAGNOSTIC VALUE OF THE CUTANEOUS TUBERCULIN TEST OF v. PIRQUET *

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Since v. Pirquet's¹ first publication, a vast amount of material has been collected concerning the anaphylactic (allergic) cutaneous test for tuberculosis. Most authors are inclined to the opinion that its value is limited; great during infancy, but during later childhood, as well as adult life, important only from a negative standpoint. It is admitted that a negative reaction is useful; it proves, except under certain special conditions that I need not refer to here, that the patient under examination has not been at any time infected with the tubercle bacillus. On the other hand, a positive reaction, after the earlier years of childhood, is believed to prove nothing save that such an infection has, at some time, occurred. It is generally accepted that the v. Pirquet reaction is as likely to be positive in a case of healed tuberculosis, as when the disease is still active. The chief argument to this effect is its occurrence in a very large proportion of apparently healthy older children and adults.

I shall here attempt to show that this adverse opinion is far too sweeping, that the value of the test has been underrated, and that the significance of a positive reaction is nearly as great in later childhood as in infancy, at least under conditions such as I have encountered.

I shall begin by reviewing some of the adverse evidence. Heim and John² found that 60 to 80 per cent. of all children above the age of infancy gave a positive reaction. Hamburger³ found a percentage of 51 at 6 years, running up to 94 toward puberty. American statistics are somewhat more favorable; nevertheless, Shaw and Laird⁴ report 45 per cent. positive after the age of 6. These data, which I could easily amplify, are certainly far from encouraging. Looking at the matter from a clinical aspect, however, the situation appears more promising; thus, Gewin,⁵ while admitting that 50 per cent. of suspected cases give a positive reaction, shows that the ratio falls to 3 per cent. among patients not suspected

*Read before the Metropolitan Medical Society, New York, April 23, 1912.

1. *Wien. med. Wchnschr.*, 1907, No. 38.

2. *Wien. klin. Wchnschr.*, 1908, No. 8.

3. *Wien. med. Wchnschr.*, 1909, No. 25.

4. *Arch. Pediat.*, July, 1909.

5. *Nederl. Tijdschr. v. Geneesk.*, 1908, v. 2.

of tuberculosis. The data of Wolff-Eisner and Brandenstein⁶ are not quite so striking; they give a positive reaction in about one-tenth of clinically non-tuberculous infants and children. More recently, Feer⁷ under similar conditions, obtained a still higher ratio, namely, 16 per cent.

The above discrepancies are sufficient to suggest that the personal equation has played a great part in these investigations, for even the last three sets of data cannot be reconciled. Assuming that the testing of apparently healthy children is purely academic, and that its results are clinically unimportant, the investigations on suspicious cases are in great need of revision, though their results have been in somewhat better accord with the clinical findings.

The following investigations, made at the Mount Sinai Hospital dispensary, include fifty cases, that fall into two groups. The first group includes children who were evidently or probably infected with tuberculosis, judging from the physical examination or symptomatology alone. The second group includes such as were below normal, but did not warrant a clinical diagnosis of tuberculosis; these children suffered from chronic cough, malnutrition, glandular enlargement, and other affections known to be frequently associated with tuberculosis, thus forming a series of cases in which some bacteriologic test should be of especial value.

My first group includes only thirteen cases, six manifestly and seven probably tuberculous. Only three were under 7 years of age. In all these cases the reaction was positive, and in four of the first six it was very intense, whereas all the other cases save one reacted only moderately. Without endeavoring to form a final conclusion from so small a material, it seems as if the intensity of the reaction stands in close relation to the severity of the infection. The chief point, of course, is the observation that not one case of certain or probable tuberculosis failed to react, and all authors are agreed that in chronic tuberculosis the proportion of negative reactions is exceedingly small.

Far more interesting is the second group, embracing thirty-seven cases, in which the children were subjected to the test because of persistent bronchitis, poor nutrition, slight adenopathy, doubtfully rheumatic joint affections, a tuberculous family history, and various other conditions that might possibly be referred to an infection with tuberculosis. The age classification of these children was as follows: Nine were under 5 years of age, the other twenty-eight ranging from 5 up to 13. Among these thirty-seven cases only two reacted positively, 5.4 per cent., a ratio almost as low as any hitherto reported, and far below the figures of Wolff-Eisner and Feer. It might be conceived that some of the discrepancy to the disadvantage of the latter is due to the inclusion of doubtful reactions,

6. Mitt. a. d. Grenzgeb. d. Chir. u. Med., 1908, v, 19.

7. Beitr. z. Klin. d. Tuberkulose, 1910, v, 18.

but Feer happens to be particularly exacting on this point. I always follow the method that I learned from v. Pirquet himself, scarifying in three places, with the control test in the middle, and using undiluted old-tuberculin. I do not see the patient again for forty-eight hours, and then record even a moderate reaction as positive. Thirty-five of my patients, therefore, did not react in the faintest degree, a most important point. I pay no attention to a reported slight reddening on the first day, which has disappeared on the second, and am sustained in this view by Feer and others, though as yet no universal agreement exists on this point. The typical reaction is quite unmistakable, persisting for a week at least. In what I call an intense reaction the erythema surrounding the papule is a half-inch in diameter, and persists for a very considerable time, even up to a month.

Confusion may arise from the recent modification of making only two scarifications. As the discomfort of the operation is trivial, I regard its curtailment in any respect as a technical error, since uncertainty should be avoided at any cost. Thus, for example, Bernheim-Karrer⁸ says that children suffering from eczema give a positive reaction. This supposed reaction may very well be due to an infection from scratching, as occurred in a nephritic patient in my service at Sydenham Hospital. In this case one of the lateral scarifications remained free, whereas a papule formed on the control test; I may add that the lesion was not exactly like the tuberculin papule, but the resemblance was nevertheless close enough to have led to confusion if the location of the papules had been different. In a day or two these lesions became excoriated; this is not a regular feature of the tuberculin papule, but nevertheless does not exclude it. I repeat that it is safest to scarify according to the methods proposed by the originator of the test.

Of the two positive cases in my second group, one patient was an Italian, a point to which I shall recur presently; the other was the sister of one of my positive patients, who herself presented no suspicious symptoms. In another family, the brother of a positive patient gave an absolutely negative reaction. It is therefore difficult to exaggerate the value of the test. Its positive as well as negative aspects are of almost equal and very great utility in diagnosis; nevertheless, the test is often regarded as beset with certain limitations, and I must discuss this side of the subject more fully.

While I have taken care to select especially unfavorable cases, excluding all children who were apparently healthy, so as to raise the positive ratio as high as possible, still my figures remain uncommonly low. I account for this by recognizing that my statistics refer chiefly to a population that is notoriously refractory to tuberculosis, and is particularly

8. Cor.-Bl. f. schweiz. Aerzte, 1910, No. 31.

free from bovine tuberculosis because of its dietary laws and the prevailing practice of boiling milk. Klose⁹ has shown that the cutaneous test furnishes no means of differentiating between the two types of tuberculosis; evidently, therefore, the relative rarity of the bovine type among my clientele would materially reduce my figures. The racial feature also is of some importance. In the children's ward of Sydenham Hospital, where many of the patients are of south Italian origin, my results have been somewhat different. While my observations there do not as yet embrace a large material, I have nevertheless noted a relatively high frequency of positive, and even intense, reactions in Italian children who were not even suspected of tuberculosis.

It would be rash to draw any conclusions from so fragmentary a study, but it seems fair to recognize that tuberculosis, latent or semi-quiescent, is far more frequent among Italian than Jewish children, and that the considerable difference in the results obtained from these two sources forms no argument against the diagnostic value of this test, but, on the contrary, emphasizes it. A positive reaction should be regarded as an important danger signal, as evidence that a tuberculous process is either still active, or likely to become active at any time, and never to be carelessly dismissed as a mere relic of a past and gone infection. Still more erroneous is the assumption that most persons, well or ill, give a positive reaction. My statistics show clearly that this is not at all the case, but that at least 90 per cent. of presumably healthy though not robust children above the age of 5 are free from any sign of present or past tuberculosis, save possibly among certain badly infected races or badly housed and fed communities.

In passing, I would make a brief reference to the Moro test, which consists in the inunction of tuberculin ointment. My experience, chiefly in private practice, shows it to be less reliable than the v. Pirquet test, as it is often negative when the latter is positive. I cannot agree with those observers who consider the v. Pirquet test too delicate for practical diagnosis; my own statistics convince me that this is not the case; of all tests it is the least equivocal and the easiest and most accurate in its application.

CONCLUSIONS

The conclusions to be derived from the above data are obvious.

If 95 per cent. of all more or less run-down children give a negative reaction, a positive reaction in the small remainder becomes highly significant. Even an older child that responds to the cutaneous test should be regarded seriously, and by no means as one of the common run; an energetic antituberculous prophylaxis should be promptly initiated, and the patient should be guarded, so far as possible, with our

9. Deutsch. med. Wehnschr., 1910, No. 48.

TABLE SHOWING ANALYSIS OF THE CASES INVESTIGATED

Age	0	1	2	3	4	5	6	7	8	9	10	11	12	13	Total
Clinical Diagnosis															
Pulmonary tuberculosis*	1	1	1	2	4
Coxitis*	1
Tuberculosis of wrist*	..	1	1	1
Pulmonary tuberculosis (?)*	2	1	4
Tuberculous adenitis (?)*	1	1	2
Tuberculous peritonitis (?)*	1	..	1	..	1
No tuberculosis !!*	1	2
Persistent bronchitis†	3	1	..	2	2	3	2	..	3	1	..	1	18
Malnutrition†	1	2	..	2	2	1	8
Chronic colitis†	1	1	2
Exudative diathesis†	1	1
Chronic adenitis†	1	..	1	2
Pleurisy†	..	1	1
Rheumatism†	1	1	2
Unresolved pneumonia†	1	1
Total Male	2	1	2	1	2	2	2	4	3	0	4	2	0	1	26
Total Female	1	1	1	1	0	3	0	3	5	2	4	2	1	0	24
Grand total	3	2	3	2	2	5	2	7	8	2	8	4	1	1	50

*Reaction positive. †Reaction negative.

somewhat limited resources, against the recrudescence of a disease which it is safest to regard at the best as latent, and by no means extinct.

Our acquaintance with the v. Pirquet test is too brief to inform us as to the relative frequency of active tuberculosis after adolescence, in individuals who seemed fairly healthy, but reacted positively to the cutaneous test in childhood. The positive determination of the tuberculo-anaphylactic state is therefore of the greatest diagnostic value, and should make our remote prognosis extremely guarded.

I append an analytical table of the material investigated.

111 West Eighty-Fifth Street.

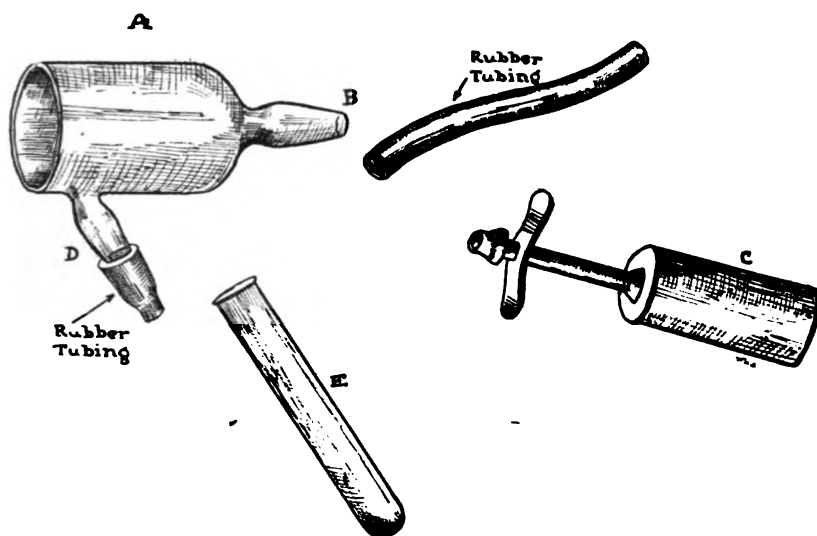
APPARATUS FOR COLLECTING INFANTS' BLOOD FOR THE WASSERMANN REACTION *

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ST. LOUIS

The methods usually employed for obtaining blood from infants are in the majority of instances extremely unsatisfactory. The veins are too small to enter and it is a tedious, difficult and painful procedure to collect the necessary amount of blood by puncturing the fingers or toes.

In European clinics use is made of a suction apparatus. This, in our hands, has proved unsatisfactory in its application to very poorly nourished infants and it is unnecessarily elaborate. The modification herein described is a simple, inexpensive device by which the necessary amount of blood can be obtained easily, with a minimum of discomfort



Suction apparatus for collecting blood for the Wassermann reaction. A, suction glass connecting at B with suction pump, C. The blood flows through D, connected by rubber stopper with an ordinary test-tube E.

to the patient and in a comparatively short space of time. The apparatus has been in daily use at the St. Louis Children's Hospital and the time spent in collecting the blood averages about two minutes.

The apparatus, as shown in the accompanying illustration, consists of a glass cylinder (A) $1\frac{5}{8}$ inches in diameter; the large end is ground

* From the Department of Pediatrics, Washington University, St. Louis, Mo.

smooth and the other end (B) is drawn out for the attachment of a small hand suction pump (C) ; an outlet (D) which is fused at an angle to the under surface of the cylinder, one-half inch from the large end, and a collecting tube (E). The collecting tube (E) fits over the outlet (D), the connection being made air-tight by means of a small piece of rubber tubing. The tube in which the blood is collected may be the size which is used in the laboratory test, obviating the necessity of transferring the blood to another tube.

TECHNIC

The technic is as follows: Connect the apparatus for use. The patient may be placed in either the upright or recumbent posture. The most convenient site is on the back just below the angle of the scapula, though any other surface of the body may be used. Having cleansed the area with alcohol and ether, one or two small punctures are made through the skin with a sharp-pointed scalpel or Hagedorn needle and the apparatus is quickly applied. With but little suction force the blood will flow from the wound through the outlet and into the collecting tube. After a sufficient amount has been collected, the tube is taken off, a cotton plug is inserted and the tube containing the blood is set aside until the examination is made. The wound is covered with a collodion dressing and the resulting swelling rapidly subsides with no discomfort to the patient.

Blood may be collected by this method from older children and adults, as well as infants, in a much shorter time and with less difficulty than by entering a vein.

The glass apparatus can be made in the laboratory or by a glass blower and the suction pump can be obtained through any surgical supply house.

1806 Locust Street.

TETANUS AS A COMPLICATION OF BURNS *

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CHICAGO

The coincidence of two cases of burns, each followed by tetanus, occurring within two days of one another, coupled with the prevalent belief as to the supposed infrequency of such a complication, formed the incentive for this report and review of the literature.

CASE 1 (Reported by courtesy of Dr. J. A. Graham).—E. F., female, 6 years old, admitted to the Children's Memorial Hospital August 23, 1911, with history that about three hours before while playing about a bonfire, she jumped too near the flames, caught her clothes on fire, and sustained a burn of the body.

Examination.—Burn of first degree, and, to a slight extent, of second degree, covering all of back from neck to buttocks, and extending around the right side to the middle line in front. Burn also of both hands, and of right upper arm. Child very nervous and irritable; cried and talked almost constantly, and at times was delirious. Pulse 112, temperature 98.8 F., respiration 24. Urine: slightly cloudy, pale color, sp. gr. 1030, acid, with trace of albumin, several hyaline casts, and a few red and white blood cells, and some epithelial cells. White blood count showed 9,500 per c.mm. Vaginal and throat smears and throat culture were negative.

Treatment.—Local dressings with picric acid, later changed to sterile vaselin with $\frac{1}{4}$ per cent. phenol (carbolic acid); strychnin sulphate, 1/100 gr. hypodermatically every eight hours; brandy m. xxx, every eight hours; soft diet, later changed to rectal feedings every six hours of 8 ounces of peptonized milk. Morphin suppository, gr. 1/12, when necessary for pain.

Course.—The child got along fairly well for about a week; the temperature ranged from 99 to 103 F.; pulse varied from 90 to 130, and respiration 25 to 40. Delirium became less pronounced, child took her nourishment, and the local condition began to improve. August 30, the eighth day after the accident, the child complained of rigidity of the jaw; later, at night, she had difficulty in swallowing. About 10 the next morning, on attempting to swallow, the jaw became very rigid, teeth set, back curved upwards, limbs extended, lips very cyanotic, and respiration stertorous and difficult. The convulsion lasted about two minutes, and recurred about every twenty minutes. At 10:50 a. m. 3,000 units of tetanus antitoxin was injected, but the convulsions were frequently repeated, the child became more cyanosed, foamed at the mouth almost constantly, and at 2:10 p. m. died in convulsions, the temperature shortly before death being 103.2 F., pulse 160, and respiration 50.

CASE 2 (Reported by courtesy of Dr. C. A. Parker).—E. H., female, 5 years old, admitted to the Children's Memorial Hospital Aug. 25, 1911, with a burn sustained a half hour before, while playing about a fire. Passers-by, in trying to extinguish the flames, dragged the child several feet on the ground.

Examination.—Burn over all of right side, front and back, extending from face and neck down to middle of thigh, the greater part being of superficial extent, and in places, of second degree. Temperature 100 F., pulse 124, respiration 28. The child was not disturbed for further examination. Urine: acid,

*Read before the Chicago Pediatric Society, May 21, 1912.

slightly cloudy, amber in color, sp. gr. 1026, with a trace of albumin, a few hyaline casts, some epithelial cells, and a few red and white blood-cells. Blood count showed a leukocytosis of 29,300. Vaginal and throat smears, and throat culture were negative.

Subsequent History.—The child was placed in a ward away from Case 1, and in charge of other nurses. Dressings of sterile vaselin were applied, morphin suppository, gr. 1/12 given for pain, aromatic cascara ordered, and liquids by mouth. The child did not sleep well, and for 24 hours passed no urine, and then only 3 ounces. The following day, August 26, the parents took the child home against advice. On September 1, the child was brought back to the hospital. The burns had been dressed every day by the family physician, fever had been present every day, child had had some constipation, later there was diarrhea, some swelling of right leg and foot, and at noon on the eighth day after the accident she complained of pain on opening the mouth. Examination showed the jaws set; the teeth could be separated only about $\frac{1}{8}$ of an inch; the child swallowed with difficulty, and some of the milk came out through the nose. At 8:40 p. m. 3,000 units antitetanic toxin was given. Child had a restless night. The next day, at 9:15 a. m., convulsion occurred, and 3,000 more units of antitoxin was injected. Her general condition became worse, attacks coming on frequently, with rigidity, difficulty of respiration, and marked cyanosis. At 2:20 p. m. a convulsion set in with twitching and jerking movements of arms and legs, rigidity of back, firmness of jaws, prominence of muscles of neck, hissing and foaming of mouth, and cyanosis; consciousness was present, although convulsion was continuous, respiration becoming more difficult, more shallow, and less frequent until death occurred at 3:28 p. m.

These two cases are noteworthy because of their coincidence, similarity in manner of occurrence, course, and result. In each instance, the symptoms of tetanus set in on the eighth day after the burn, and the complication proved fatal about twenty-six hours after its appearance.

A review of the literature available shows that tetanus is not an infrequent occurrence after burns, for forty-seven cases are reported with more or less detail, and mention is made of about twenty others; these, with the two reported above, make a total of sixty-nine cases. Those which are mentioned only, include two cases by Rose,¹ four by Taylor,² two by Lockwood,³ eleven by Norris,⁴ and one by Billroth.⁵

A tabulated summary of the reported cases is given herewith.

From a study of the data furnished by these forty-nine cases, the following facts are noted:

With Reference to Season.—Tetanus may arise as a complication of burns during any month of the year, but it is more common during the colder months. The mortality rate, however, is somewhat higher in the warmer months. From November to April, inclusive, occurred 74 per cent. of the cases, with a mortality of 73 per cent.; 26 per cent. of the series came in May to October, inclusive, and of these 83 per cent. died.

Sex.—The condition is met with equal frequency in the two sexes. The chances for recovery are one in five for females, and one in four for males. Of the forty-nine cases, twenty-five were in females, with five recoveries, and twenty-four in males, with six recoveries.

Age.—The complication may present itself in patients of all ages; the youngest case recorded is that of a boy of 4 years, the oldest is that of a woman 64 years of age. It is most common between the ages of 11 and 20. Eighteen per cent. of the cases occurred during the first decade, about 33 per cent. during the second decade, 26 per cent. in the third, 18 per cent. in the fourth, and 4 per cent. in the sixth. It proved fatal in all those above 35 years of age, in 87 per cent. of those between 11 and 20, and in about 75 per cent. of the remaining ages.

Location of Burn.—In 40 per cent. the trunk was involved together with the upper, or lower, or all of the extremities; in 25 per cent. the lower extremities only; in 17 per cent. the upper only; in 10 per cent. the trunk alone, and in 6 per cent. the head and face. The mortality is greatest when tetanus complicates burns where the trunk is involved, either alone, or with burns of other parts of the body, for 87.5 per cent. of the patients so burned died. When either the upper or the lower extremities are injured, or the head and face alone, the chances of recovery are about one in three.

Period of Incubation.—The interval between the date of burn and the onset of tetanic symptoms varied from twelve hours in one instance to four weeks in two other cases. In thirty-three cases (67 per cent.) the complication appeared within the first twelve days. Of these, more than 90 per cent. were fatal. In the remaining sixteen cases, tetanus set in after the twelfth day, and eight (50 per cent.) recovered. Of four cases coming on after the third week all got well.

Duration.—The complication may run either an acute or chronic course; the extremes noted in this series are five hours in one case and six weeks in another, but the majority terminate within ten days. Of the forty-nine cases, thirty-seven (75 per cent.) ended within the first ten days after the onset of the tetanic infection, and of these, sixteen cases (32 per cent.) terminated within forty-eight hours. Of the thirty-seven cases, all but one died; in the remaining twelve cases, the course ranged from two to six weeks, and ten patients recovered.

PROGNOSIS

Of the forty-nine patients, thirty-eight died and eleven recovered, making a mortality rate of 77 per cent. Death usually occurs within the first week after tetanus makes its appearance. The prognosis is less favorable in cases occurring in the warmer months of the year, in adult life, where the trunk is involved, and when the incubation period is short (less than twelve days).

SYMPTOMATOLOGY

Tetanus may set in after a burn, regardless of its location, extent, or degree. The earliest and most frequent symptom is a stiffness of the jaws with a consequent difficulty in opening the mouth and in swallowing;

SUMMARY OF REPORTED CASES OF TETANUS FOLLOWING BURNS

Case	Date	Sex	Age	Part of Body Involved	Incubation*	Duration*	Result	Remarks
1	Oct. 10, 1836 ^a	F	13		13	6	D	
2	April, 1841 [†]	M	32	Feet	30?	21	R	Assafetida every 2 hrs. gr. v, by mouth, or ½ oz. of tr. per rectum
3	Nov. 6, 1846 ^a	F	9?	Right lower extremity (deep)	10	36 hr.	D	
4	Nov. 10, 1846 ^a	F	25	Right arm (superficial)	18	8	D	
5	Dec. 28, 1846 ^a	F	19	Upper extremity and back (superficial)	9	5	D	
6	Apr. 10, 1848 ¹⁰	F	30	Back (superficial)	16	4	D	
7	Jan. 30, 1849 ¹¹	F	12	Trunk, face and arms (superficial)	9	5	D	
8	Feb. 1, 1849 ¹²	F	17	Waist and left lower extremity (severe)	8	36 hr.	D	
9	Jan. 25, 1852 ¹³	F	8	Chest and arms (severe)	15	3	D	During a paroxysm, glottis remained so long closed that laryngotomy was performed
10	Nov. 15, 1852 ^a	F	11	9	4	D	
11	Feb. 15, 1853 ¹²	F	10	Trunk and right arm (severe)	11	10 hr.	D	
12	Feb., 1853 ¹⁴	M	4	Head, chest, left upper extremity (severe)	9	14	R	Dover's powd. gr. 2 Sesquiox. iron gr. 4 every 4 hrs.
13	Oct. 7, 1853 ¹⁵	F	36	Right buttock (superficial)	12	3	D	
14	Dec. 4, 1853 ¹⁶	F	64	Trunk and lower extremities (severe)	8	14 hr.	D	Epileptic
15	Jan. 22, 1854 ¹⁵	M	12	Trunk and arm (severe)	12	64 hr.	D	
16	Feb. 9, 1854 ¹⁷	F	9	Face and arms	7	24 hr.	D	
17	Feb. 19, 1855 ¹³	F	38	Right lower extremity (severe)	12	6	D	
18	Apr. 5, 1855 ¹⁸	F	9	Upper trunk and arms	9	5 hr.	D	
19	—, 1858 ¹	M	25?	Lower trunk (severe)	16h	6 hr.	D	
20	Oct. 16, 1859 ¹⁹	M	24	Left arm, chest, and hip	11	3	D	Epileptic
21	Mar. 19, 1861 ¹	M	34	Thighs (severe)	4?†	14	R	
22	Apr. 9, 1861 ²⁰	M	18	Arms	10	3	D	
23	Apr. 9, 1861 ²⁰	M	16?	Arms	20	?	D	
24	Jan. 14, 1862 ¹	M	32	Lower extremities (severe)	11	2	D	
25	Feb. 19, 1866 ²¹	M	40	Chest and lower extremities (severe)	9	20 hr.	D	Alcoholic
26	Apr. 2, 1869 ²²	M	12	Lower extremities	12	7	D	
27	Jan. 1, 1874 ²	M	31	Head	10	6	D	Epileptic

*In days, unless otherwise specified. †Weeks.

SUMMARY OF REPORTED CASES OF TETANUS FOLLOWING BURNS—(Continued)

(Case)	Date	Sex	Age	Part of Body Involved	Incubation*	Duration*	Result	Remarks
28	—, 1875 ²	F	14	Back and thighs (severe)	9	24 hr.	D	
29	July 1, 1875 ²	M	18	Left elbow (superficial)	4	16	D	
30	June 9, 1877 ²³	M	22	Head, face, arms chest (severe)	9	2	D	
31	Nov. 28, 1878 ²⁴	F	12	Trunk and extremities (severe)	7	8 hr.	D	T. 104.6 F. at time of death
32	Dec. 22, 1878 ²⁵	F	26	Left hand and chest (severe)	8	20	R	Epileptic. Amputation of hand
33	Dec. 5, 1882 ²⁶	M	22	Extremities (severe)	18	36	R	Large doses of KBr, chloral hydr. and morphin.
34	Dec. 9, 1886 ²⁷	M	12	Extremities (superficial)	4	10	D	
35	Jan. 1, 1887 ²⁸	F	24†	Left leg, arm, and thorax (severe)	21	42	R	Frequent doses of morph. acet. 87 gr. in 35 days
36	—, 1889 ²⁹	M	60	Knees (severe)	14	60 hr.	D	
37	Feb. 20, 1893 ³⁰	M	30	Right leg and foot (severe)	8	7	D	Venesection. Behring's serum, 4 injections, 20 gr. each
38	Nov. 2, 1894 ³¹	M	9†	Leg and forehead (slight)	14	21	R	Tizzoni antitoxin, 12 injections, 5 and $\frac{3}{8}$ gm.
39	Nov. 12, 1894 ³²	M	15	Lower extremity (deep)	11	10	D	Six injections of antitoxin, 111 gr.
40	June 26, 1895 ³³	M	39	Chest and extremities (severe)	10	42 hr.	D	
41	Dec. 27, 1898 ³⁴	F	12	Right arm and axilla	14	15	R	12 injections in 9 days of 110 c.c. antitoxin
42	May 7, 1900 ³⁵	F	40	Trunk, face, arm (superficial)	19	36 hr.	D	
43	June 17, 1900 ³⁶	M	30	Left lower extremity (severe)	21	8	R	7 m. phenol q. 3 hrs. subcutaneously
44	Feb. 23, 1902 ³⁷	M	30	Chest	12	4	D	Intracerebral injection of 3 cm. serum
45	Dec., 1906 ³⁸	F	25	Left arm (slight)	12	17	R	2 c.c. of 2 per cent. phenol sol. hypo. for 10 days, every 4 hrs.
46	June 6, 1909 ³⁹	F	19	Face, chest, upper extremities (severe)	19	25	R	Antitetanic toxin; lumbar puncture
47	June 20, 1909 ⁴⁰	M	24	Head, face, trunk, arms (severe)	17	4	D	
48	Aug. 23, 1911 ⁴¹	F	6	Trunk and upper extremities (superficial)	8	26 hr.	D	Antitetanic toxin
49	Aug. 25, 1911 ⁴²	F	5	Right side (superficial)	8	26 hr.	D	Antitetanic toxin

*In days, unless otherwise specified. †Weeks.

this is soon followed by pains and rigidity or spasms of the muscles of the neck, back, abdomen, or limbs. Within twelve to twenty-four hours, there may occur opisthotonos, risus sardonicus, cyanosis, and profuse sweats. In children, delirium and restlessness may be present. Fever is always noted, and in some instances may be very high just before the fatal termination (107.1 F. in Case 44), and it may persist for two hours or more after death (104.7 F. two hours after death in Case 37). The respiration is rapid, labored, and shallow, and the pulse small and frequent, especially toward the end. Consciousness may remain undisturbed until death ensues. This was noted in five patients, including one of the author's cases. There may be constipation. The urine shows no marked changes; the blood may be normal or present a leukocytosis. Death occurs from exhaustion, or because of spasm or paralysis of the muscles of respiration.

Post-mortem examination of those cases which came to autopsy revealed no unusual pathologic findings.

TREATMENT

Aside from the local treatment of the burn, alleviation of pain, attention to the bowels, and the use of supportive measures, it would be well, in view of the possibility of tetanic infection, to give patients in all cases of burns a prophylactic injection of antitoxin. None of the cases reported were so protected against the complication. When tetanus has set in, the value of antitoxin may be questioned. In this review, of the eight cases (37, 38, 39, 41, 44, 46, 48, and 49) in which the patients were treated with antitetanic serum, only three recovered (Cases 39, 41, and 46). As the incubation period in two of these cases was fourteen days, and in the third, nineteen days, and as it has been shown that in cases developing after the twelfth day the patients have an even chance of getting well regardless of the treatment employed, the part played in these recoveries by the serum is rather uncertain.

Two patients were treated with phenol, and both recovered; one (Case 43, incubation of twenty-one days) received subcutaneous injections of 7 minims of phenol every three hours, for eight days, some relief being obtained after four doses; the other (Case 45, with tetanus twelve days after the burn) was given 2 c.c. of a 2 per cent. solution of phenol hypodermatically (Bacelli's method) every four hours for ten days.

Two cases recovered under large doses of morphin; one of these (Case 33, incubation eighteen days) got as much as 6 gr. of morphin sulphate a day, and the other (Case 35, incubation twenty-one days) received morphin acetate in one-fourth to 1 gr. doses, taking from $1\frac{3}{4}$ to $6\frac{1}{2}$ gr. in twenty-four hours, and in thirty-five days, a total of

87 1/6 gr. Another patient (Case 32, incubation eight days) had an amputation of the infected hand performed six days after the onset of tetanus, and the woman recovered.

CONCLUSIONS

1. Tetanus is not an infrequent complication of burns.
2. The mortality is greater in cases occurring in the warmer months of the year.
3. Tetanus complicating burns involving the trunk is more serious than when the burn is on other parts of the body.
4. The longer the incubation period the less the mortality.
5. The greatest number of fatalities occurs early in the complication.
6. The prophylactic injection of tetanus antitoxin is advisable in all cases of serious burns.

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AN UNUSUAL LESION OF THE RIGHT CRUS IN AN INFANT OF FOUR MONTHS

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A case rather confusing to the practitioner, yet highly interesting because of its comparatively rare occurrence but far reaching effect, is that one of a young child brought to me for examination by Dr. Burnett.

History.—E. P., aged 4 months; Italian. The infant's mother and father were alive and well. One sister of the patient, 18 months old, was enjoying good health. The mother had had no miscarriages, the father denied specific infection and there was no history of tuberculosis in the family.

The child was born after a period of normal gestation and after an uneventful confinement. Labor was easy and of short duration, no instruments were used and there is no history of trauma. He had been fed on the breast and, with the exception of an occasional vomiting spell, which the mother attributed to "too much milk," the infant had had no grave physical disturbances.

The mother noticed that after the child was born the left eyelid drooped and that he did not move his left leg and arm as much as the right leg and arm. When three months passed without visible improvement the child was taken to Dr. Burnett, to whom I am greatly indebted for the privilege of examining this interesting condition.

Examination.—Physical examination showed a well-nourished child of four months with a ptosis of the left eye-lid and a left hemiparesis. He was able to move both his eye-balls in all directions. The pupils were unequal in size; the left being but a pin-hole which reacted to neither light nor accommodation but dilated quickly when one drop of 2 per cent. cocain was applied. The optic disks were normal. There was no involvement of other cranial nerves. Distinct weakness of the left arm, but more so of the left leg, was manifested. The left abdominal reflex was less active than the right and the left knee-jerk was stronger than the right. There was no ankle clonus. The Babinski sign was present on both sides (quite proper for a child of four months) and, so far as could be ascertained, sensation was normal.

During the two months previous to the preparation of this report the child had shown no material change. He was still in the same condition in which the mother saw him at birth and presented a left ptosis, a left immobile pupil and a left hemiparesis.

The difficulty in tracing these stigmata to the root lies in the fact that the exact anatomic relations of the individual nuclei of the oculomotoris are still a matter of dispute. That its complexity is not understood is not at all surprising when one recalls how large a number of muscles the third nerve innervates; how these muscles are anatomically and physiologically

dependent on each other and how close a relation they bear to other groups of nerves necessary to call forth proper co-ordination. Although studied by such noted investigators as Spitzka,¹ Starr,² Edinger,³ Westphal,⁴ Von Gudden,⁵ Obersteiner,⁶ Barker⁷ and others, adequate information concerning these various parts has not been forthcoming.

The lower neurons of the oculomotoris possess cell bodies which are situated in the nucleus nervi oculomotoris located in the pons. On section it is seen to occupy a position in the tegmentum, ventral to the aqueductus cerebri, just dorsal to the longitudinal fasciculus and inclined at an angle to a line drawn parallel to the long axis of the fourth ventricle. The axons of each nerve are mainly from the nucleus of the same side, but also partly from the nucleus of the opposite side; that is, there is a partial decussation. This decussation contains the fibers mainly from the posterior or distal (spinal) third of the nucleus. The nuclei of the third nerve are very complex and consist of numerous groups of cells. Their appearance can be well shown by reconstruction such as that produced by Meyer or Sabin. By this reconstruction method the nuclei are seen to be in the shape of an arrow with its head ventralward and its shaft dorsalward.

In the case presented, interest lies mainly in the probability of a decussation of the third nerve by these decussating fibers. Perlia⁸ and Von Koliker,⁹ as well as Bernheimer,¹⁰ have proven conclusively that there may be a decussation in man. Other investigators have shown that it exists in animals and birds. As a result many attempts have been made to localize the nucleus and root-fibers corresponding to individual eye muscles. The crossed fibers go through the fasciculus longitudinalis in its dorsal part and after a somewhat curved course pass near the lateral border of the red nucleus when, turning inward, they are traceable toward the medial and lateral portion. Starr found that the fibers to the ciliary muscles arose in the posterior portion of the medial group and that from

1. Spitzka, E. C.: The Oculomotor Centers and Their Coordinators. *Jour. Nerv. and Ment. Dis.*, 1888, xv, 413.

2. Starr, M. A.: Ophthalmoplegia Externa Partialis; *Jour. Nerv. and Ment. Dis.*, 1888, xv, 301.

3. Edinger: *Verl. der central. Hörnervenbahnen*, *Arch. f. Psychiat. u. Nervenkr.*, 1885, xvi.

4. Westphal: Ueber die chronische progressive Lähmung der Augenmuskeln-Supply, *Arch. f. Psychiat. u. Nervenkr.*, 1891, xxii.

5. Von Gudden: *Gesammelte Abhandl.*, Wiesbaden, 1889.

6. Abersteiner: *Anzeig. d. k. k. Gesellsch. der Aerzte in Wien.*, 1880.

7. Barker: *The Nervous System*, New York, 1901.

8. Perlia: Die Anatomie des Oculomotoriuscentrums beim Menschen. *Arch. f. Ophth.*, 1889, xxxv: Sec. 287-308.

9. Von Kolliker: *Sitzungsb. d. Phys-med. Gesellsch. zu Würzb.*, 1892.

10. Bernheimer: Das Wurzelgebiet des Oculomotorius beim Menschen, viii, Wiesbaden, 1894.

the lateral portion arose the fibers to the levator palpebræ. On the other hand, Kahler and Pick stated that the pupillary fibers ran in the anterior bundles and that the fibers to the extrinsic muscles ran in a lateral and medial group. Schwabe,¹¹ who has attempted to trace out these fibers along lines suggested by Von Gudden, states that the fibers governing the levator palpebræ superioris and retrahens bulbi could not be connected with any cells. He is rather of the opinion that they are possibly innervated by cells in the most lateral dorso-distal group of the nuclei of the opposite side.

These notes, applied to the case above presented, permit argument. Since it presents a left ptosis, a left immobile pupil and a left hemiparesis the following inferences suggest themselves as possible explanations. First, we may here be dealing with an unusual case of an uncrossed pyramidal tract with a lesion in the crus in the region of the third nucleus. This deduction seems rather improbable when one recalls the exceedingly rare occurrence of such a condition. Second, there may be an agenesis, an aplasia or hypoplasia of the nuclei of the fibers that innervate the iris and Mueller's muscle. This agenesis would condition one lesion and the disturbance of the pyramidal tract would be another distinct condition. This seems far more probable because agenesis of the nuclei or portions of the nuclei are rather frequent occurrences, as is proven by pathologic examinations. Third, the lesion involves, and the one to which the writers feel more free to accept, the crossed fibers of the right third nerve in the posterior and distal portion, which is in close proximity to the pyramidal tract. Should this be so (and one of us is inclined to believe it is), the case would seem to justify Schwabe in his contention that it is possible that the fibers of the levator palpebræ come from the posterior and lateral portion of the nucleus of the opposite side and pass in close proximity to the pyramidal tract.

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11. Schwabe: *Neuro. Centralbl.*, 1896, xv.

THE STANDARDIZATION OF BLOOD PRESSURE READINGS
BY MEANS OF AN AUTOMATIC DEVICE FOR
INDICATING SYSTOLIC AND DIASTOLIC
PRESSURES IN CHILDREN *

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One cannot but be struck with the variation in systolic and diastolic blood-pressure readings on the same individual as recorded by different observers. In a recent test three separate observations were made on a series of ten patients, by three groups of observers working independently. The patients were in bed, did not change position between readings and the observations were all taken within half an hour. Each group of observers was supplied with a similar instrument. The first set used the older method of estimating systolic pressure by tactile pressure over the radial artery with the oscillation of mercury as the indicator for the diastolic pressure; the second group used the auscultatory method for both systolic and diastolic pressure, while the third employed the auscultatory method for systolic pressure and the Fedde pith-ball indicator for the diastolic. The observers were familiar with the apparatus, being accustomed to taking blood-pressures as a daily routine in the ward.

The results were astonishing. The widest variation in systolic pressure was 30 mm. mercury; that of diastolic, 40 mm. of mercury, while there was found a variation of 25 in the reading of mean pulse-pressure. In but few of the cases did two groups agree throughout and in none did all coincide exactly. The observers were equally experienced, none of them being experts in blood-pressure readings, but all had average ability.

It is evident, therefore, that with our present methods of blood-pressure reading at the bedside, there enters an element of variation which may be called the personal equation. In those observers who have served a long apprenticeship in the art of blood-pressure reading, this variation is small, while in those less expert it may be considerable.

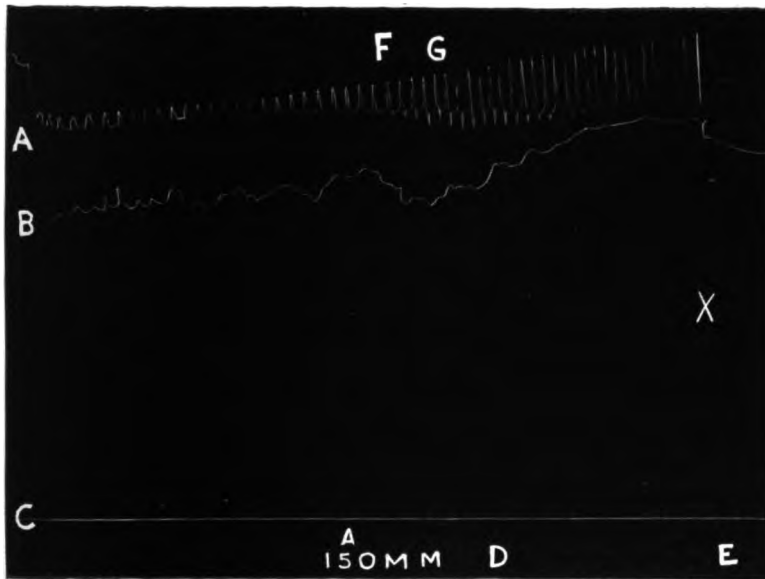
In the every-day use of an instrument, this variation is approximately the same, and in comparative readings is of little consequence. But in absolute observations, especially those used for publication, this variation must be considered.

*Read in the Section on Diseases of Children of the American Medical Association, at the Sixty-Third Annual Session, held at Atlantic City, June, 1912.

About a year ago I devised a method by which the systolic and diastolic pressures could be both visibly and automatically indicated, and published a description of it,¹ to which article those interested are referred for details.

During the past winter this instrument has been in constant use both in hospital and private work and has proved very reliable. In a long series of observations taken daily on many patients the variations have been extremely small, both in systolic and diastolic pressures, each day's observations being recorded without any knowledge of the previous day's readings.

The indicating device was tested against the readings of the Erlanger sphygmomanometer, the two instruments being connected in one circuit.



Blood-pressure tracing. A. Erlanger tracing. B. Plethysmograph tracing. C. Base line for indicating time of first movement of pith-ball. D, Point at which pith-ball first moved. E, End of experiment. F, Point of systolic pressure on Erlanger tracing. G, Point on Erlanger tracing at which pith-ball moved.

At the same time the arm was placed in a plethysmograph with recording needle leading to the tambour, on which was recorded the tracing of the Erlanger instrument. One of these tracings is herewith presented.

In the figure the uppermost tracing is from the needle of the Erlanger instrument, the middle one the plethysmograph, while the lowest line is that of the electric timer. On the last-named line is a break indicating the first movement of the pith-ball which occurred when the mercury

1. Hoobler, B. R.: *Med. Rec.*, New York, December 30, 1911.

registered 150 mm. in the Erlanger instrument. Farther along on the base line is the point indicating the end of the experiment. If one measure back from this point on the base line to the break at 150 and likewise measure back the same distance on the tracings of both the Erlanger instrument and of the plethysmograph, one will note the coincident phenomena indicated by them. It will be seen that the amplitude of the tracing of the Erlanger instrument has widened considerably, indicating that the point of systolic pressure is found slightly earlier by the Erlanger tracing than by the pith-ball indicator. On the plethysmograph tracing it will be noted that there is a gradual raising of the lever as the arm fills with blood. In six consecutive tracings made in this manner the systolic pressure was read at 150, 152, 150, 148, 148 and 146.

It is my experience that by means of this visible indicating device the systolic blood-pressure may be read with the same accuracy as obtained when using the more complicated instruments. By thus eliminating the variation due to personal equation, which may be great or small, according to the observer's experience, blood-pressure readings may be standardized.

This device was originally designed for taking blood-pressures in children, which is very difficult owing to the small size of the arms and the difficulty in obtaining uniform results either by tactile or auscultatory methods. Where the arm is too small for use, the cuff may be applied to the leg. The leg readings in children are from 10 to 15 mm. mercury higher than in the arm. It can, however, be used just as readily in adults as in children and may be attached to any type of instrument, mercurial or aneroid.

Therefore this device possesses the following advantages:

1. Automatically and visibly indicates systolic and diastolic pressure.
2. It compares very closely in efficiency with the Erlanger instrument.
3. It enables one to eliminate the variation due to personal equation, which has been shown to be considerable in different observers.
4. It is of especial use in children in whom blood-pressure readings are difficult, since it permits the use of the leg when the arm is too small.

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TUBERCULOSIS OF THE MESENTERIC GLANDS IN INFANTS AND YOUNG CHILDREN; ITS EFFECT ON ABSORPTION *

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Our conception of tuberculosis in early childhood has been modified by the work of various investigators, whose experiments seem to show that the common channel of infection is not so much the air passages, as the intestinal mucosa. The tubercle bacilli may pass through the intestinal wall, be carried by the lymphatics to the mesenteric glands, and thence into the thoracic duct and blood stream. These views do not reject the older hypothesis that the bacilli are borne by dust into the lungs.¹ Von Behring² says that "the milk fed to infants is the chief cause of consumption," but he also says that it is absolutely important to keep a coughing consumptive away from a nursing infant.

Corner³ finds tuberculous mesenteric glands in the majority of children on whom he has performed a laparotomy, and believes that a large percentage of children have such lesions. He explains this relative frequency as follows: There is a stage of digestion in which there is an abrupt change in the mechanical and physical processes at the time of transition from a rapidly moving liquid fecal material of the small intestine, to a more slowly-moving, solidifying fecal mass of the large intestine. The point of transition is at the ileocecal valve where there is a temporary pause and the bacterial flora have an opportunity to multiply rapidly. Cultures taken here and at other parts of the intestinal canal have shown that there are many more bacteria in the ileocecal region than elsewhere. Nature has furnished a large amount of lymphoid tissue in this region to combat the organisms which are presumably in their most infectious stage. He assumes, therefore, that the ileo-cecal valve is the most likely place of entrance of the tubercle bacilli. The lymph-follicles of the small and large intestines also serve as points of entry.⁴ The report of the Royal

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¹Read in the Section on Diseases of Children of the American Medical Association, at the Sixty-Third Annual Session, held at Atlantic City, June, 1912.

1. Riviere, Clive: Phthisis in Children, *Lancet*, London, Jan. 15, 1910.

2. Von Behring: *Suppression of Tuberculosis*, New York, 1904.

3. Corner: *Tuberculosis of the Mesenteric Glands in Children; Its Nature and Treatment*, *Lancet*, London, 1912, 1, clxxxii, 426.

4. Hof, Carl: *Ueber primäre Darmtuberculose*, Kieler Dissert., 1903; Hausmann, V.: *Ueber Fütterungs Tuberculose*, Berlin. klin. Wehnschr., 1903, No. 7, quoted from Von Behring (Note 2).

Commission on Tuberculosis⁵ had twenty-nine cases of primary abdominal tuberculosis of which fourteen yielded the bovine type of bacillus, thirteen the human type and two were proved to contain a mixture of the bovine and human tubercle bacillus. There is, therefore, very good evidence that cows' milk is one of the common sources of contagion. Those familiar with babies and small children have frequently seen the variety of dirt that is picked up off the floor and swallowed, and cannot be surprised that the human type of tuberculosis also plays an important part.

The bacilli are carried by the lymphatics to the mesenteric lymph-nodes where they may lodge, eventually cause caseation and destroy the usefulness of these nodes and lymph-channels for digestion and absorption. If a sufficient number of the glands are destroyed, absorption through the lymphatics will be impossible and a dam will be placed across the channel through which certain foodstuffs gain entrance to the blood-stream and the rest of the body. It is necessary to review the manner in which the three great classes of foodstuffs, fats, carbohydrates and proteins, are absorbed.

Fats.—The majority of fats eaten by young children are in the forms of neutral fats. During the course of digestion they are hydrolized into fatty-acids and glycerin and, if they come in contact with alkaline intestinal juices, the fatty-acids combine with the salts and become soaps. They pass through the intestinal mucous membrane, and are taken up in the lymphatics as neutral fats, and are carried through the thoracic duct to the blood. If the lymph of the thoracic duct is collected, it shows only 60 per cent. of the fat which is absorbed from the intestine. It is not known, however, what happens to the other 40 per cent., but experiments have made it probable that it is not absorbed directly into the blood.* Any obstruction to the flow of lymph would, therefore, interfere with the absorption of fats.

Carbohydrates.—All carbohydrates are changed during digestion into monosaccharids, which are absorbed in the small intestine before they reach the ileocecal valve. The percentage of sugar in the thoracic duct does not increase during digestion of a meal rich in carbohydrates, while there is a definite increase in the percentage of sugar in the portal system.⁷ These facts indicate that sugars are absorbed entirely by the blood of the portal system and not by the lymphatics.

Protein.—Numerous experiments make it probable that the proteins are taken up entirely by the blood of the portal system and that they are not absorbed through the lymphatics because during a meal rich in protein

5. Final Report, Part I, p. 13, London, 1911.

6. Starling in Oppenheimer's Handbuch der Biochemie des Menschen und der Tiere, iii, 2, pp. 225-6; Jena, 1909.

7. Starling: (See note 6) p. 241.

there is no appreciable increase in the flow of lymph or in the amount of protein which it contains.⁸

Physiology shows, therefore, that if the mesenteric lymph-nodes become diseased enough to block the entire flow of lymph, the protein and carbohydrate digestion and absorption will not be interfered with. At least 60 per cent. of the fat ingested may not be absorbed. The amount of interference with the absorption of fat would naturally depend on the number and location of the diseased glands and how completely they blocked the lymph-ducts and their numerous anastomoses.

Berggrün and Katz⁹ describe the occurrence of fatty stools in tuberculous peritonitis and give a review of the literature up to 1891. Schmidt¹⁰ describes a case of an 8-year-old girl, with intestinal and mesenteric tuberculosis, in whom all of the mesenteric glands proved to be caseous. The stools were diarrheal and contained a great deal of fat. Fr. Müller's¹¹ case, a child 4 years old with phthisis and caseation of the mesenteric and retroperitoneal lymph-nodes, had yellow-gray, mealy stools which showed under the microscope many fat crystals. These stools contained 42 per cent. of fat. Wietrand¹² performed metabolism experiments in a case of tuberculosis of the intestine and found that 35 per cent. of the fat-ingested was lost in the feces. Wharton¹³ says that in case of *tabes mesentericus*, "Absorption from the intestine becomes greatly diminished, the child greatly emaciated, the abdomen is distended, and an insatiable appetite, diarrhea and offensive stools are the chief symptoms."

I studied the cases reported in this paper with special reference to the digestion of fat, carbohydrates, and protein. The methods of examining the stools were those described in a previous paper.¹⁴ The diet was modified according to the results of these examinations.¹⁵ The findings may be summed up as follows: The cases were clinically typical cases of tuberculous peritonitis with positive von Pirquet skin reactions, in three of which the diagnosis was confirmed by laparotomy, and two more by autopsy. Meat and starch were digested in a normal manner, while fat appeared in the stools in a large excess in every case except one. In this instance, Case VI, it was fair to assume that the lymphatics were not entirely blocked. It was found that if fat was given in the food in large amounts, eventually the stools would change from a formed, apparently

8. Starling: loc. cit. Note 6, pp. 233-4.

9. Berggrün and Katz: *Wien. klin. Wchnschr.*, 1891, No. 4, p. 858.

10. Schmidt: *Ztschr. f. exper. Path. u. Therap.*, 1909-10, vii, 270.

11. Müller, Fr.: *Untersuchung über Icterus. Ztschr. f. klin. Med.*, 1887, xii, 86.

12. Wietrand: *Die Bedeutung des quantitativen Stoffwechselversuches, etc., Die Heilk.*, 1898-99, ii, 67.

13. Wharton: *Osler's Modern Medicine*. Phila. and New York, 1908, p. 823.

14. *Archives of Pediatrics*, 1911, xxviii, No. 2.

15. Morse and Talbot: *Intestinal Indigestion in Children*, *Am. Jour. Med. Sc.*, June, 1910.

well-digested stool into a diarrheal, acid stool containing much mucus, and that signs of a secondary intestinal indigestion would appear. An example of this is Case X. This is presumably due to the fact that the excessive amounts of fat in the intestine are acted on by the intestinal bacteria whose action causes putrefaction. The stools often have the odor of rancid butter. As tuberculosis developed in Case VIII, the character of the stools changed. In the earlier stages fat was digested in the normal manner, and later a great deal was lost in the feces presumably because tuberculous mesenteric glands entirely blocked the lymphatic system.

The diet of these children should be regulated according to the stool-findings, and in all instances in which the disease has progressed far enough for the tuberculous processes to block the lymphatic system, fat should be removed entirely from the food, and the caloric needs of the child be supplied by carbohydrates and protein. When this is done the patient is usually much more comfortable, as was Case X, and the body has a better opportunity to combat the disease. In one instance, Case II, there was distinct improvement in the appearance of the child and she gained one-half pound in one month's time.

CASE REPORTS

CASE 1.—Catalina C., aged 9 years, M. G. H. O. P. D. No. 182906, entered the hospital Nov. 6, 1911, complaining that she was debilitated and anemic for one year. There was no known exposure to tuberculosis and she had never been sick aside from symptoms referable to her stomach. She was brought in by the school nurse because she did not look well. The diet included macaroni, cocoa, pork and other foods of a similar nature. On questioning it was found that she had seven or eight stools a day.

Physical Examination.—This showed a fairly developed and poorly nourished, pale girl with a distended abdomen, diastasis of the recti, shifting dullness in the flanks and a fluid wave. There was slight general tenderness over the whole of the abdomen, but no masses were felt there. The circumference of the chest at the nipple was 60 cm. and of the abdomen over the umbilicus 63 cm. The physical condition was normal elsewhere except for moderate emaciation. The von Pirquet skin tuberculin test was positive. The diagnosis of tuberculous peritonitis (serous form) was made. Two days later examination of the stool under the microscope showed an excess of fats mostly in the form of fatty acids. Fat was removed entirely from the diet, and under careful dieting the stools dropped from 8 a day to 3 a day. The circumference of the abdomen on entrance was 63 cm. over the umbilicus, and one month later was 60 cm. and the fluid diminished in amount. When last seen there was no fluid wave, and the child reported that she was much better in every way.

CASE 2.—Carilda R., aged 20 months, M. G. H. O. P. D., No. 189977, entered the hospital March 12, 1912. One other child in the family died one month previously at the age of 4 years with "ascites." The child was breast fed for fifteen months and perfectly healthy until about one month prior to admission, at which time the mother noticed that the baby began to be limp and listless. Although she did not complain of pain she preferred to lie down most of the time. The abdomen became more and more prominent and recently tender. The stools had been hard, yellow and constipated. The diet consisted of whole milk, macaroni, rice, cereals and oranges.

Physical Examination.—This showed a poorly developed and nourished, pale child with a prominent, distended abdomen which was tympanitic throughout.

A large mass was felt extending across the upper part of the abdomen corresponding to the course of the transverse colon; this mass was tender. The von Pirquet skin tuberculin test was positive. The diagnosis of tuberculous peritonitis (fibrinous form) was made. Two days later the stool was recorded as loose, pinkish-brown and it contained large particles of orange pulp. Under the microscope there was no meat or starch, but there was a large excess of fat in the form of soaps. She was given a diet without fats and in the course of one month gained one-half pound. Although the general condition remained the same, the baby looked much better under careful dieting.

CASE 3.—Ralph W., age 4 years, M. G. H., No. 176350, was admitted to the hospital May 30, 1911. There was no known exposure to tuberculosis. As a baby, he was breast fed for three months and after that on the bottle. About six months prior to admission the stomach began to swell up and he complained of general abdominal pain, without vomiting. Four weeks ago the abdomen became considerable larger and the abdominal pains more marked. The bowels were slightly constipated.

Physical Examination.—This showed a poorly nourished, colored boy with an anxious expression. The muscles were flabby. The lungs were resonant, but contained many fine, medium and coarse rales. There was no change in the respiratory murmur. The level of the abdomen was a little higher than that of the thorax; it was tense but not tender. There were several masses the size of olives in the right lower quadrant, and no shifting dullness. There was an umbilical hernia which was excoriated. The diagnosis of tuberculous peritonitis and bronchitis was made and he was put on the "house diet" of the children's ward. This consisted of meat, vegetables, whole milk, bread, butter, cereals and cooked fruits. The stool was small, dark greenish-brown and semi-solid, with a moderate amount of mucus intermixed. Under the microscope it showed a moderate excess of fat in the form of soaps. There was no meat or starch. Eleven days later the stool was medium sized, light brown and reacted acid to litmus paper. Under the microscope it showed a large excess of fat in the form of soaps. Four days later the fats were partially removed from the diet, i. e., skimmed milk was given in place of whole milk and butter, and the stools showed very much less fat. He was discharged to his parents ten days later with a practically normal stools.

CASE 4.—William C., aged 2 years, M. G. H., No. 176419 was admitted Jan. 2, 1911. There was no family history of tuberculosis. The child was breast fed for sixteenth months and for the last four months had been eating milk, egg and a little bread. About three months prior to admission it was noticed that he was getting thin and "wobbled" as he walked. One month latter the abdomen began to increase in size and for the past ten days had been tender. No cough or vomiting; bowels regular.

Physical Examination.—This showed a poorly developed and nourished boy who was irritable and frightened; his muscles were flabby and more or less atrophied. The level of the abdomen was higher than that of the thorax; it was rigid, tense and somewhat tender. There was shifting dullness and a fluid wave. The umbilicus was reddened, indurated and with superficial excoriations; hard masses extended from it for about 4 cm. in all directions. There were also masses, the size of which were not reported, in both the left and right lower quadrants. The physical examination otherwise was normal. The diagnosis of tuberculous peritonitis (serous type) was made and he was given the "house diet" of the children's ward—meat, vegetables, whole milk, bread, butter, cereals and cooked fruit. The stool was large, yellow, firm and sour, the scraped surface being greasy. It contained no blood or mucus, but under the microscope there was a moderate excess of fat in the form of soaps. Two days later the umbilicus suddenly began to discharge a stream of pus which became fecal in character. This was opened and found to be a large, extra-peritoneal abscess. The diet was regulated as in Case 3.

CASE 5.—Evelyn R., aged 4 months, M. G. H., No. 173935, was admitted Jan. 12, 1911. The mother was at a sanatorium being treated for tuberculosis, and very little was known about the baby except that she had been fed mostly on the bottle.

Physical Examination.—This showed a poorly developed and nourished child with a facial paralysis on the right side of the face, and a discharge from the right ear underneath which there were several large lymph-nodes. The lungs were normal except for a few fine râles in both backs. The abdomen was large and somewhat resonant, with a protruding umbilicus. There was no rigidity, spasm or masses. The physical examination was otherwise negative. She was put on a formula which figured 2.75 per cent fat, 6.00 per cent sugar, and 1.50 per cent. protein; $4\frac{1}{2}$ ounces every three hours, seven feedings. The stool two days later was small, greenish-yellow, with no curds or mucus. The reaction was alkaline and under the microscope it showed a large excess of fats. The von Pirquet skin tuberculin test was negative. Four days later after the food had been regulated according to the stool findings, i. e., the fats were reduced to 2.00 per cent., the stool was reported as small, normal in appearance, of alkaline reaction and containing under the microscope a small amount of fat in the form of soaps. The baby died January 22, and the necropsy report was as follows:

*Necropsy.*¹⁶—Esophagus and stomach on section are normal. The large intestine is not remarkable. The walls of the small intestine are generally pale, but in several places show small, dark reddish areas dotted over with tubercle-like points. One of these areas is situated in the region of the ileocecal valve and the others, beginning at a point about 30 cm. above the ileocecal valve, are scattered along the ileum. The mesenteric lymph-nodes generally are enlarged and studded with smaller and larger yellowish caseous masses. These caseous glands are in close relation with the dark reddish tubercle-studded area in the wall of the ileum. On section the mucosa of the ileum shows, opposite the dark reddish areas mentioned, small losses of substance with reddish, rather ragged margins and bases, the latter showing tubercle-like points. There are about a dozen of the ulcers lying transversely and the largest is about 1 cm. in greatest dimension.

The retroperitoneal lymph-nodes in the region of the pancreas and lesser omentum are enlarged and show many minute to small yellowish caseous masses.

Diagnosis.—The anatomic diagnosis was as follows: Tubercular ulcers of the ileum; tuberculosis of the mesenteric and retroperitoneal glands; miliary, focal and caseous pneumonia of the lungs; tuberculosis of the liver, spleen and adrenals; solitary tubercle of pia-arachnoid; solitary tubercle of the aorta; streptococcus septicemia.

CASE 6.—Charles P., aged 3 years, M. G. H., No. 177457, was admitted July 27, 1911. There was no history of tuberculosis. The baby was breast fed for one year, at which time he had measles followed by bronchopneumonia. After that the diet was the ordinary diet of the age. For the previous three months he had complained of pain in the epigastrium. The abdomen was swollen, especially in the upper part. He had lost considerable weight but had never vomited. The bowels were regular.

Physical Examination.—This showed a well developed and nourished child with the appearance of perfect health. The abdomen was very prominent, tympanitic, with a general tenderness and spasm. There was no shifting dullness, no fluid wave or masses. The physical examination was otherwise normal. Two days later an indefinitely defined mass was felt across the upper part of the abdomen just above the umbilicus. The von Pirquet tuberculin skin test was positive. The diagnosis of tuberculous peritonitis (fibrous form) was made and he was given the "house diet." The stool was normal in appearance and contained no blood or pus. Under the microscope it showed a small amount of fat in the

16. This autopsy report was kindly given to me by Dr. Oscar Richardson of the Massachusetts General Hospital.

form of soaps. This was probably not in excess. After the child became used to the hospital the mass in the upper part of the abdomen was made out and corresponded more or less to the position of the transverse colon. A laparotomy performed August 4 showed a dry, tuberculous peritonitis with tubercles and numerous adhesions throughout the abdominal cavity. No observation was made of the condition of the mesenteric glands. Presumably these glands were more or less affected. The examination of the stool, however, makes it probable that the lymphatic system was not entirely blocked because there was not an excess of fat in the stools. It was not necessary to modify the diet in this instance because the boy digested and absorbed his food in a normal manner.

CASE 7.—Clarence N., aged 15 months, M. G. H., No. 178582, was admitted September 20, 1911. No known exposure to tuberculosis. He had always been bottle fed. Had had a slight cough for three weeks, and had been really sick for the previous week. The bowels and urine had been apparently normal. He breathed very rapidly and vomited practically all food. The physical examination showed that the lungs were resonant throughout and normal, except for many coarse and fine rales especially at the left base. The abdomen was full, distended and tympanitic. There was a slight general spasm but no masses or shifting dullness. The physical examination was otherwise negative. The von Pirquet skin tuberculin test was positive two days later. A tentative diagnosis of tuberculous bronchopneumonia was made and he was given a diet of whole milk and cereals. There was no more vomiting. The stool on October 10 was yellowish-green with considerable fine mucus, but no curds, pus or blood. Under the microscope there was a large excess of fat in the form of soaps. On October 15, after the diet had been regulated according to the stool-findings, i. e., skimmed milk was given in place of whole milk, the stool was greenish-yellow with a small amount of mucus and under the microscope a slight excess of soaps; it contained no tubercle bacilli.

The baby died October 21, and the necropsy was as follows:

*Necropsy.*¹⁷—Esophagus, stomach and small intestine on section are normal. The large intestine shows in its mucosa in the region of the junction of the cecum and first portion of the ascending colon an oval loss of substance with fairly smooth, rounded, slightly irregular margins which descend rather abruptly and deeply to a rather thin, grayish base which is slightly rough and irregular in its central portions. The large intestine elsewhere is not remarkable. The ulcer situated near the mesentery and the mesentery in this region show several small nodes, and a short distance from this a large mass of mesenteric nodes about 5 by 4 by $4\frac{1}{2}$ cm. over all. On section of the large mass much caseo-pus is yielded, and a cover-glass specimen from it shows numerous typical tubercle bacilli. The section surfaces of the glands show discrete and confluent smaller and larger yellowish, homogeneous areas. The mesenteric glands elsewhere are visible but show no good evidence of any tuberculosis. The retroperitoneal glands are not remarkable. The lungs and other organs are normal.

Diagnosis.—The anatomic diagnosis was tubercular ulcer of the large intestine; tuberculosis of the mesenteric lymph-nodes; miliary tuberculosis of the spleen and liver; streptococcus septicemia.

CASE 8.—Samuel F., aged 3 years, M. G. H., No. 177995 and No. 179067, was admitted Aug. 28, 1911. No known exposure to tuberculosis. For the previous six weeks the patient had been failing; had had slight cough and fever all the time, and for the past three days his abdomen had gradually increased in size. He had lost a great deal of weight, and his appetite had been very poor.

Physical Examination.—This showed a poorly developed and emaciated child with distinct pallor. His abdomen was large and very prominent, the level being above that of the thorax. It was tympanitic throughout, and had a slight

17. Autopsy by Dr. Richardson, Massachusetts General Hospital.

"doughy" feeling. There were no masses or shifting dulness. The superficial veins were very much distended. While taking the "house diet" the stools were brown, homogeneous and formed; there was no blood, pus or mucus and under the microscope no excess of fat or starch. The von Pirquet tuberculin skin test was mildly positive. The physical examination was otherwise normal.

Between September 18 and October 30 he had diphtheria. October 30 the physical examination was practically the same as at first noted. The stool, however, was brown, full and reacted alkaline to litmus paper. It contained many coarse, undigested particles, and under the microscope showed a large excess of fat in the form of soaps. The fat was then removed from the food, and there was marked improvement in the character of the stools. November 2 a laparotomy showed a small amount of fluid pus and on exploration a large mass of lymph-nodes the size of marbles in the mesentery. The intestines were adherent to the peritoneum just above the incision. The surgeon made a diagnosis of tuberculosis of the peritoneum and mesenteric glands.

CASE 9.—Thomas B., aged 5 years, M. G. H., No. 180665, was admitted Jan. 23, 1911. There was no known history of tuberculosis. The child was brought in because he had been found pale and thin for one week. The abdomen was much enlarged and tender. The appetite was good until the previous day. The diet was not good, as he ate candy, pie, cake and other foods from the table.

Physical Examination.—This showed a well developed and fairly nourished, pale boy. The abdomen was full, distended and tympanitic throughout. There was a slight tenderness on pressure and marked shifting dulness in the flanks, but no fluid wave. The von Pirquet skin tuberculin test was markedly positive. After he had been on the "house diet" three days, the stool was dark brown, soft, very foul; no neutral fats or fatty acids; there was a large excess of soaps. And again, on January 31, after the fat had been removed from the food, the stool was pasty, pale and still contained a large excess of fat.

CASE 10.—I. T., a girl, 4½ years of age, was first seen Aug. 24, 1911. There was no known history of tuberculosis. In January, 1911, she had measles and did not recover satisfactorily; the Moro skin test was done and found to be positive. At that time she had a little cough and was examined by four physicians in a sanitarium for tuberculosis. These men could find no evidence of tuberculosis of the lungs. The radiograph of the chest also showed no sign of tuberculosis. Her appetite was never hearty. About the first of July she developed a diarrhea which persisted. She lost a good deal of weight. On examination she was found to have a positive von Pirquet skin tuberculin test, and the stools under the microscope showed a large excess of fats.

Physical Examination.—This was normal except that the abdomen was slightly prominent, especially in the lower part. In the right iliac fossa there was a mass the size of a small peach and just to the left and below the umbilicus was a second mass the size of an olive. There was a slight indefinite resonance all over the abdomen, but no spasm of tenderness. A few days later, on a diet free from fat, the stool was large, greenish, with many flecks of mucus. Under the microscope there was a slight excess of fat, no starch or meat fibers. There was a very large number of pus cells. A stained smear showed no tubercle bacilli.

The feces were injected into a guinea-pig which was killed six weeks later and found to contain many tubercle bacilli.

Whenever even smaller quantities of fat were given, the stools became more frequent, and had the odor of rancid butter, and there was marked distress. The coincident discomfort would destroy the appetite so that at times she would eat practically nothing. As long as the fat was removed entirely from her food she lived in comparative comfort up to the time of her death two months later.

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HISTORY OF THE CLASSIFICATION OF GASTRO- INTESTINAL DISEASES IN ANCIENT AND MODERN TIMES *

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The nutrition of the new-born infant is not a new subject, and the diseases of the digestive tract and the intestinal disturbances of infancy, we may assume, are as old as the race.

It has been thought that on this occasion an historical retrospect of gastro-intestinal disorders would be of interest; especially at this time when new hypotheses are appearing in certain quarters as to the nature of gastro-intestinal disorders in infants, and since some of the views which were held a decade ago are being subjected to sharp attack. It is obvious that a scientific classification depends on exact knowledge.

HISTORICAL

In reviewing the literature from the earliest period to the present time, we find great variation in clinical description and in the interpretation of the gastro-intestinal disturbances of infancy. The classifications, in so far as they have been made, have been influenced by the prevailing thought of the period. In ancient and medieval times when medical knowledge was simple and when fundamental facts in anatomy, pathology and physiology were meager or unknown, classification of disease was elementary and imperfect. In the anatomico-pathologic period the profession was possessed by the thought that every disease must have not only a distinct anatomic location, but must be represented by gross anatomic and histologic changes in tissue and cells. Virchow pronounced the dictum that every physiologic type must have its pathologic prototype. With him, cellular pathology was sufficient to explain disease processes of almost every kind. With the advent of the bacteriologic era, the flora of the gastro-intestinal tract was most assiduously studied. Normal and abnormal organisms were discovered, but it was soon found that bacteriologic investigation had its limitations. It was settled for all time that some gastro-intestinal diseases were definitely due to bacteria, but it was shown also that there was a group of infantile intestinal

*Chairman's Address: Read in the Section on Diseases of Children of the American Medical Association, at the Sixty-Third Annual Session, held at Atlantic City, June, 1912.

diseases which seemed to bear no definite relation to the nature, number or kind of bacteria. Then began the investigations of food and the physiology of their digestion, perversion of digestion, studies in metabolism, and the effect of anomalies in the constitution of the individual in so far as they could affect digestion and nutrition. Classification, then, of the gastro-intestinal diseases of infancy at any period, can consist only of a systematic arrangement of the knowledge of that period. A real classification can be made only when a sufficient number of facts are accumulated to explain the nature of the disease processes. It is evident, too, that the various arrangements into groups of diseases reflect the prevailing medical opinion of the time. Progress has been slow; the labor and energy which has been expended in the study of this disease group has not been in vain and need not be done over again. If the anatomico-pathologic findings are insufficient to explain the facts, then possibly the bacteriologic investigations may shed more light. If the latter are insufficient, then possibly chemical and physiologic investigations may assist in unraveling the mysteries of the difficult problems which present themselves. It is important, then, that we study this disease group in historical retrospect, lest we be carried away too far by the enthusiasm of the present, forgetting the labors which have already been performed, the facts which have been accumulated and the positive and negative evidence which has been presented to us by those who have preceded.

Diseases of the mouth, especially aphthous stomatitis, were described by Hippocrates, and in more recent times by Billard. Thrush was recognized by Soranos about 200 A. D. Nutrition of infants and children was discussed by the ancient East Indians. They directed that emetics be administered once weekly and laxatives once monthly. Historians tell us that East Indian physicians found that breast milk was not secreted for the first three days. During this interval they advised that the infant be given salt and butter, or honey — with the view of producing mild catharsis. In case of failing mother's milk, a wet-nurse was to be secured when the infant was 10 days old. They cautioned, however, that the wet-nurse should undergo a careful examination by a physician. It appears that this necessary evil, wet-nursing, was in vogue among the well-to-do class in ancient India as it is with us to-day.

After the first month it was the custom to give the infant a sweet paste to suck. The infant was weaned at the sixth month, we are told, and after this time was fed rice, sour milk, and after the third year meat from goats and fowl, with butter and honey.

Very important are the writings of Soranos (Ephesian) 200 A. D. Chapters 24 to 40 of his works reflect the knowledge of children's diseases of his time, but also contain improvements and suggestions of his own. He advises, for example, that the mother should not nurse too frequently

or too long, and during the night the mother is directed to nurse the infant as little as possible. Large wet-nurses produce better milk than small ones. He describes finger-nail and water tests for breast milk. Onions, fatty and highly spiced foods are condemned because they will produce deleterious effects in the breast milk. Excessively fat milk, Soranos thought, was capable of working injury to the infant because it could not find its way through the small intestinal apertures. Almost modern seems his caution not to rock or shake the baby after nursing because it produces a condition like sea-sickness. He warns against frightening children, and devotes two chapters (39 and 40) to dentition and weaning. It is probable that the disorders of dentition were the subject of discussion in his day. He held, however, that scarification of the gums was unjustifiable. He believed in simplified therapeutics and discarded the then prevalent custom of administering urine as a remedy, and warned against too vigorous manipulation in mouth washing. In the treatment of thrush the bare finger should not be used, but should be well covered.

Dr. Ludwig Unger in 1904 compiled a monograph entitled "The Child Book," Bartholamäus Metlinger (1457-76), being a history of children's diseases in the middle ages. This is the earliest German pediatric publication. The work is of doubtful scientific value, and reflects the scholasticism and the mysticism of the middle ages. The second part of Metlinger's work treats of the nourishment of children, and also of the infant who cannot nurse at the breast; it tells how a wet-nurse may be secured and how the infant may be weaned. He believes that the milk is produced from the blood of the mother which flows through the veins into the breast and milk is formed in some indefinite way. Concerning the digestive disturbances of infants he says that indigestion is produced among children by an excessive quantity of milk which they cannot take care of.

Somewhat later, 1540, Sebastiano Austrio considered under separate headings flatulence, humid or white flow, diarrhea, cholera and diarrhea and vomiting, and Thomas Phayre in 1551 in a book, "The Regiment of Lyfe; Whereunto is Added a Treatise of the Pestilence with the Booke of Children; Newly Corrected and Enlarged"; "Febleness of the Stomacke and Vomiting" gives him opportunity for some philosophic thought. "Colyke and rumblings of the guttes cause the child restlessness. He crieth and frettith itself and many times also makes urine by reason of winde that oppresseth the neck of the bladder."

The period that we are referring to seems to be marked by the lack of uniformity in classification. Various writers show no common view concerning the underlying causes of diseased conditions. A vague symptomatology for the most part was the basis for description. Thus Sylvius

Francisco mentions "gripes of the belly due either to wind or from sour and sharp humours."

Gaulteri Harris, 1671, thinks that all the symptoms of gastro-intestinal disorders owe their origin to acid products in the body. He gives no classification of the gastro-intestinal diseases, though speaks of vomiting and diarrhea in a general way, caused by the presence of acids. Even in modern times the theory of acid intoxication has played an important part in explaining the pathogenesis of gastro-intestinal disorders.

A little later we find John Astruc, 1746, attempting a classification on the nature or appearance of the stools. Thus he speaks of stercoral, cœliac, lenteric and dysenteric stools. Worms receive a great deal of attention in this treatise, and he finally concludes that worms are not due to spontaneous generation, but that they are produced from eggs.

Nicholis Rosen von Rosenstein, a Swedish physician (1706 to 1773), a professor in Stockholm, was an active and versatile writer on practical subjects. He followed in the footsteps of Lars Roberg. Rosen gave instruction in clinical medicine and his "Diseases of Children" was popular in his own country and in England for a long time. Rosen divided the gastro-intestinal diseases into constipation, rectal prolapse, flatulence, abdominal pain and colic. The classification is based entirely on symptomatology and he proceeds to subdivide diarrhea into fourteen different varieties.

During the eighteenth century the knowledge concerning pathology and nature of gastro-intestinal diseases of children remains vague. The remarks of Roswell Park (*An Epitome in the History of Medicine*) are pertinent. He says that in reviewing the theories, as well as the lives of the medical luminaries of the eighteenth century, one experiences a feeling of mingled respect and disappointment; respect for the devoted way in which they worked, and sought for the truth, and disappointment at so much waste of intellectual power and labor. The lesson is taught also, and should be impressed, that in all the so-called new systems, old principles for the most part reappear, and that the labors of the past are rarely so deliberately consulted as to guard against repetition and revamping of the theories that had long before been proved futile.

William Moss, 1781, wrote an essay on "The Management and Nursing of Children in the Earlier Period of Infancy," and lays great stress on "Gripes, with or without Looseness."

Eberle, 1783, was the first to consider in detail the colic of infants.

Michael Underwood, 1789, classified the gastro-intestinal diseases in a purely symptomatic manner. He says that "the true watery gripes is esteemed the most dangerous of all purgings and is usually thought fatal; if the purging continue for a few days the stools are very thin and numerous. The child looks wretchedly and everything it takes runs

almost immediately through it." This condition is not unlike the cholera infantum of the later writers.

Christoph. Girtanner, 1794, refers to the work of Benjamin Rush on infantile cholera.

In 1773 Dr. Benjamin Rush gave a description of the symptoms of cholera infantum and the discussion of its etiology and treatment. He thought that the disease seldom appeared in Philadelphia until the middle of June, generally continued until near the middle of September; and its frequency and dangers are always in proportion to the heat of the summer. The observations of Rush were soon corroborated by his contemporaries and his successors in America and abroad.

THE ERA OF SCIENTIFIC METHODS

The nineteenth century is distinguished by the introduction of more purely scientific methods. This is the century of Darwinism, Spencer, Huxley and Heckel. Roswell Park says that the discoveries of botany, the results of better knowledge of natural history and more accurate habits of study have influenced modern progress not a little, and have led to better classification and broader knowledge. The development of the laws of physics, more accurate knowledge of physiology and anatomy, extension of the knowledge of chemistry and zoology, have exerted a wide influence on the methods of study and on the introduction of modern scientific thought.

John Cheyne, 1802, wrote a very painstaking account of icterus and described a condition which he designates as green scours, and atrophica ablactatorium, or weaning brash. The latter was an atrophic condition caused by the weaning of children too suddenly and at an unfavorable season of the year. He performed autopsies on these cases and records that they correspond to cases of cholera infantum described by Rush.

In 1821 Adolph Henke published infant mortality statistics. He believed that half of all the children born died before the age of 10 years.

C. M. Billard, 1828, was trained in the anatomic school of France, and made a specialty of the diseases of children, and his publications were important and epoch-making. He divided diseases into a group which considered the functions of the organs, and into a second group which treated of disorders associated with organic lesions. He described diarrheas and the gastric and intestinal disorders.

William Potts Dewees, 1836, an American writer, divided the diarrhea of infants into seven varieties and described each in considerable detail. To illustrate: In the biliary form of diarrhea the stools are loose, copious and of a bright yellow or green. The mucous variety he thinks is caused by a sudden checking of perspiration, or sudden application of cold to the body or feet. He closes with a consideration of cholera infantum and asserts that the disease is peculiar to this country.

Alois Bednar published an important work in 1850. He discusses diseases which are based on abnormal processes, or decomposition of foods ingested into the alimentary tract, and disorders of the gastro-intestinal tube which are based on anatomic changes of the tissues. Bednar's classification was based on wide clinical observations and pathologic investigations. His descriptions were comprehensive and exerted a strong influence on the thought of the period.

The book of Barthez and Rilliet, 1855, indulged in considerable speculation as to the nature of softening of the stomach; and considers softening of the stomach and intestines separately. They divide the diseases into three sections. The first, primary catarrhal; second, secondary catarrhal, and a third group in which the causes are of doubtful catarrhal origin but are non-inflammatory.

J. Forsyth Meigs, 1848, recognized the fact that the diseases which involve the stomach are usually associated with similar lesions of the intestinal tract, and are little likely to occur alone. He makes two classifications, one functional and the other degenerative; the latter attended with appreciable anatomic lesion.

J. Lewis Smith, 1869, considers non-inflammatory diarrhea, and the intestinal inflammation of infants.

Edward Henoeh in 1862 discusses dyspepsia and divides it into acute and chronic forms. Of the intestinal diseases he considers cholera infantum, catarrhal diarrhea, dysentery and constipation.

The climax of this period is represented in greatest detail by the writings of H. Wiederhofer, 1880. Wiederhofer was associated in his work with Professor Kundrat of the Pathological Institute of Vienna. Wiederhofer was inspired by the clinical insight of his Vienna predecessors; Kundrat by the excellent traditions of Rokitansky, and of the Pathological Institute of Vienna. These writings represent the anatomico-pathologic era in the classification of gastro-intestinal diseases of infants. The classification is a long and painstaking one, including diseases of the stomach and intestines. Wiederhofer in an ingenious way endeavors to reconcile pathology and anatomy with general symptomatology and his own bedside observations. The observations were acute and unerring; clinical descriptions were painstaking; there were wide gaps in the knowledge concerning causation and interpretation.

Jacobi in 1887 contributed a valuable monograph classifying diseases into gastric and intestinal affections, and in a paper published somewhat later considers the infective causes of intestinal diseases, particularly dysentery. In his earlier publication he advocates the use of cane sugar in lieu of milk sugar. He suggests, under certain conditions, the use of beef or mutton broth, and takes occasion to say that it is not the chemical

formula alone which determines the rank of a substance as a nutrient. The digestibility of the food must be considered.

Biedert, 1878-1894, gives it as his opinion that the cause of gastro-intestinal disease of infants in the majority of cases is due to food. He lays great stress on a condition which he terms fat diarrhea, and he recommends a classification based on the appearance of the stool. He considers in detail overfeeding, the diseases due to decomposition of proteins, diseases due to excessive fat feeding, and a group of disturbances produced by excessive sugar, especially as it occurs in breast milk.

Baginsky represents the transitional period from the anatomic-pathologic to the bacteriologic era. He thought that micro-organisms were not specific; nevertheless, the common saprophytic bacteria of the intestines were capable of taking on virulent activity and becoming the pathogenic microorganism; though foreign bacteria may gain access to the gastro-intestinal tract these bacteria may, according to Baginsky, wander from the intestine into other organs, such as the kidney; they are rarely found in the circulating blood. He says the severest disturbances are caused by the action of bacteria on the foodstuff, producing fermentation and toxic products.

The labors of Booker, of Lesage and Escherich did not show any specific microorganisms for the diarrheal diseases. Escherich considered that gastro-intestinal diseases might be due to ectogenic and endogenic causes. The ectogenic gave rise to toxic gastric catarrh, while the endogenic caused infection of the chyme, with dyspepsia. After all the labor no specific organism was found.

Bacteriologic research was of value, though it was negative. The bacteriologists themselves conceded that other lines of research might yield greater reward. Investigators turned their attention from bacteriology to the chemistry of food, and studies in the physiology of digestion. Experiments in metabolism were inaugurated in many quarters.

MODERN CLASSIFICATIONS

The American Pediatric Society in 1894 offered a classification. The classification is very extensive. The enteric diseases are divided into non-inflammatory and inflammatory. The non-inflammatory may be mechanical, such as dilatation of the colon, prolapse of the bowel and polypi. The classification is very extensive, though in many instances and of necessity non-committal. It is complicated and seems difficult of practical application at the bedside.

From all that has gone before, it is evident that the digestive disturbances of nurslings were in the past classified variously according to the progress of physiology, pathology and bacteriology. The oldest classification was based on symptomatology. One would suppose that pathologic research and knowledge would have led to a simpler classification. This,

however, was not the case. Referring to the classification of Wiederhofer in 1880 and Baginsky in 1884, it is seen at a glance that they were not inclusive. The pathologic knowledge was vague and in most cases indefinite. It was also observed that one and the same pathologic lesion was associated with a varied or inconstant clinical course. Thus it was noted that inflammatory conditions as a basis for classification of the digestive disorders in infants resulted in disappointment. Terms like catarrh, gastric catarrh, intestinal catarrh, gastritis, enteritis, are used in a confusing way and require considerable elucidation in every instance, and pathologic conditions were persistently assumed which did not really exist. As improvement in pathologic investigations and technic occurred, lesions which were supposed to exist could not be confirmed. Although bacteriologic research furnished interesting and valuable information concerning normal process in the digestive tract, it did not afford data for classification of pathologic process of gastro-intestinal disorders. Thus bacteriologic classification failed. Some authors attempted to refer all digestive troubles to bacterial action, and when the ectogenic causes of diseases could be excluded, then the normal endogenic microorganisms of the intestinal tract were supposed to be capable of taking on pathologic activity and producing the disease in question. Czerny and Keller insist that aside from the intestinal disorders which are explained by pathology or by bacteriology, there are many disturbances of nutrition which could be understood only by a knowledge of infantile metabolism. All three modes of investigation are of the greatest importance and none should be used exclusively while others are neglected. Since the most enlightened students of this disease group cannot accept a bacterial cause for the entire group of gastro-intestinal diseases, it is necessary to divide them into two classes:

1. Those diseases which are evidently bacterial in origin.
2. Those in which there is no evidence of a bacterial infection.

It is a well-known fact that bacteria take part in all the normal processes of digestion. This does not imply that they are always causal factors in disease. This very fact led Czerny and Moser in 1894 to make a general classification into two groups — dyspepsia and gastro-enteritis. Czerny and Keller in their *Ernährungsstörungen* say that the names of the two groups were unfortunate because they have been employed by other authors in former times with various meanings. Nevertheless, the basic idea was accepted and was finally made use of in the classification of the Pediatric Section of the Paris International Medical Congress, 1900. Czerny and Keller insist that the digestive disorders of infants should be separated from those of older children. This was in contrast to the older writings of Wiederhofer and Baginsky. Czerny and Keller propose the following classification:

1. Digestive disturbances *et alimentacione*.
2. Digestive disturbances *ex infectione*.
3. Digestive disturbances through congenital anomalies.

CLASSIFICATION OF FINKELSTEIN

The historical résumé would be altogether incomplete without a brief reference to the recent teachings of Finkelstein; therefore, without going into detail into material which is fresh in every one's mind, I shall in the briefest space possible give a short synopsis of his contribution. His classification is the last one to be offered, it is based on researches into the chemistry of food, studies in metabolism, together with careful clinical analysis. He divides the subject as follows:

1. Weight disturbances characterized by a diminished tolerance for milk, especially milk fat. The infant does not thrive. The weight is stationary as a rule. The bowel movements are hard, dry and formed.

2. Dyspepsia is a more severe disease manifestation than the foregoing. It is characterized by a diminished tolerance not only for fat but also for carbohydrates. Such children do not gain in weight; they tend to suffer from diarrhea, and fail to increase in weight even if the diet is increased, constituting the so-called paradox reaction.

3. Decomposition, a condition characterized by marked loss in weight, low temperature, slow pulse. The loss in weight continues even when considerable food is administered; easily infected, or infection takes place readily. A marked intolerance for fat and carbohydrates is present. These infants are subject to secondary infectious processes, as furuncles, abscesses, etc.

4. The next clinical group is alimentary intoxication, characterized by fever, disturbances of consciousness, albuminuria, rapid superficial breathing, great intolerance for food, particularly for sugar and other whey constituents.

In considering the disturbances produced by breast milk, he refers to underfeeding as well as the dyspepsia produced by overfeeding. Disturbances of nutrition on account of congenital perversions of the constitution receive attention; for instance, he discusses the neuropathic constitution, the exudative diathesis and errors in development as factors influencing digestion and nutrition. He also considers the effect of quantitative changes in food which refers to overfeeding and underfeeding. Passing next to qualitative changes he pays particular attention to the injuries produced by starch. He devotes a chapter to parenteral infection and insists that infants suffer infections because food tolerance has been lowered by disturbances of nutrition, the lowered resistance which results in consequence making infection possible. He concludes with a chapter on the infections of the gastro-intestinal tract though he believes that parenteral infections are more frequent than genuine gastro-

intestinal infection. He concludes by saying that knowledge of the gastro-enteritis of infants, so far as bacteriologic facts are concerned, is only slightly developed, and consequently present views are subject to considerable changes in the future. He devotes a chapter to infections, gastro-enteritis, typhoid, septic infection and concludes with a short chapter on colitis.

DEDUCTIONS

One cannot fail to be impressed with several salient points as he skims hastily over the progress of the ages: First, the changing views depend on advance in knowledge and the variation in human thought during different periods. The sound logical reason of one age has yielded to mysticism, speculative philosophy and humoral pathology of another age. In some instances those whom we consider the ancient saw more clearly than medieval thinkers. Whither are we drifting now? Are we standing on firm foundation, or are we again on the quicksands? Has all the work in cellular pathology been completed? Has it shed all its light? Is the biologic study of the gastro-intestinal tract forever a closed book? Are all of the questions that confront us in the solution of this group of disorders to be disclosed by chemical study of food and the more complicated inquiries into the metabolic changes? The danger is lest we drift too far. Is it not well that occasionally we take inventory of the debts which we owe the past as well as the contribution of the present? We see light from the researches of to-day, though the illumination is not sufficient to permit us to say that all darkness has vanished.

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STUDIES IN THE BACTERIOLOGY OF THE ACUTE INTESTINAL DISEASES OF INFANCY *

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The relationship of bacteria to the acute intestinal diseases of infancy is a study that has attracted many workers and yet to-day the problem is far from being answered in a satisfactory manner. Several reasons exist for the indefiniteness of the views that are held at the present time, chief among them being the variance in the bacteriologic findings, the failure to distinguish between the presence of bacteria and the action of bacteria, and the unsuccessful attempts which have been made to correlate the laboratory findings with the different clinical types of intestinal disturbance. Much of the early work is at present of value only for its historical interest, as the more recent advances in bacteriology have shown the earlier differentiation of organisms and methods of study to have been incomplete.

In the earlier days of bacteriology numerous organisms were reported as the cause of dysentery epidemics. In 1888 Chantemesse and Widal¹ described a short bacillus which was later claimed by Widal to be identical with *B. dysenteriae*. Maggiori² reported several organisms from Italy in 1892, and in the same year Ogata³ described a Gram-positive organism in Japan. Two years later Silvestri⁴ contributed a diplococcus and Arnaud⁵ a colon bacillus-like form. In 1895 Celli and Fiocca⁶ reported the streptococcus and an organism resembling the colon bacillus which Celli⁷ subsequently claimed to be identical with the Flexner type of dysentery organism. Janowski⁸ reached the conclusion from his studies that no one organism was the cause of dysentery. This same view was held by those workers who studied the intestinal flora of infants.

*From the Department of Medical Research, University of Pennsylvania, Philadelphia.

1. Chantemesse and Widal: *Gaz. méd. de Paris*, 1888, No. 16.
2. Maggiori: *Centralbl. f. Bakteriöl.*, 1892, xi, 173.
3. Ogata: *Centralbl. f. Bakteriöl.*, 1892, xi, 264.
4. Silvestri: *Riforma med.*, 1894, No. 22.
5. Arnaud: *Ann. de l'Inst. Pasteur*, 1894, viii, 495.
6. Celli and Fiocca: *Centralbl. f. Bakteriöl.*, 1895, xvii, 309.
7. Celli and Valenta: *Centralbl. f. Bakteriöl.*, 1899, xxv, 481.
8. Janowski: *Centralbl. f. Bakteriöl.*, 1897, xxi, 88.

Among them Booker,⁹ who studied the subject for a number of years, stands out most prominently. From a bacteriologic standpoint he separated out two groups of cases, one a "bacillary type" which he considered as probably due to the *Proteus vulgaris*, and the other a group of more severe cases in which streptococci were found. Escherich¹⁰ and his pupils likewise made quite extensive studies but found no one organism in constant association. By some of the earlier writers the *B. coli* was considered of etiologic importance and even more recently Apfelstedt¹¹ has written in support of this view. Williams and Cameron,¹² Escherich,¹⁰ Cook,¹³ Cooley¹⁴ and others have described the *B. pyocyaneus* in association with epidemics of dysentery in infants, and other organisms such as the *B. acidophilus* (Salge¹⁵) and *B. perfringens* (Sittler¹⁶) have been reported. Kendall and Smith¹⁷ in 1911 reported three cases in which they found *B. aerogenes capsulatus*, the association of which with the dysenteric condition they consider of importance. Practically all of these studies were made before the discovery of the dysentery bacillus by Shiga in Japan and Flexner in Manila, and hence no conclusions of any importance can be drawn from them.

DYSENTERY ORGANISMS

The discovery of the *B. dysenteriae* in epidemics of dysentery in various parts of the world, and the subsequent attempts to correlate these organisms with the various types of intestinal disturbance peculiar to infancy, necessitates a special study of this group of organisms. It is unnecessary for our purpose to repeat the history and early controversies in regard to the identity and unity of the organisms, as it is at the present time accepted that there is a group of closely related bacteria differing slightly by cultural and agglutination reactions which may be grouped together under the term *B. dysenteriae*.

The following classification has been quite generally accepted, and although a number of other types and subvarieties have been described, it suffices for our purposes. It may be that some of the subvarieties are mere mutations as Müller¹⁸ claims to have observed.

9. Booker: Arch. Pediat., 1890, vii, 92; Johns Hopkins Hosp. Rep., 1897, vi, 159.

10. Escherich: Wien med. Wchnschr., 1897, x, 917; Deutsch. med. Wchnschr., 1898, xxiv, 633; Jahrb. f. Kinderh., 1899, xlix, 137.

11. Apfelstedt: Therap. Monatsh., 1906, xx, 473.

12. Williams and Cameron: Jour. Path. and Bacteriol., 1896, iii, 344.

13. Cook: Jour. Am. Med. Assn., 1904, xliii, 1933.

14. Cooley: Jour. Am. Med. Assn., 1908, l, 607.

15. Salge: Der akute Dünndarmkatarrh des Säuglings, Leipzig, 1906.

16. Sittler: Centralbl. f. Bakteriologie, 1908, Orig. xlvii, 551.

17. Kendall and Smith: Boston Med. and Surg. Jour., 1911, clxiv, 306.

18. Müller: Centralbl. f. Bakteriologie, 1904, Ref. xlii, Part 57.

		FERMENTS				
A	I	Man- nite	Dex- trose	Saccha- rose	Mal- tose	Shiga or Shiga-Kruse "New Haven."
	II	+	+	—	—	'Y' (Hiss and Russell) "Seal Harbor."
B	III	+	+	+	—	Strong (Manila).
	IV	+	+	+	+	Flexner or Flexner-Harris "Baltimore" (Duval).

The first variety — Shiga — is culturally distinguished from the remaining three (Group B) by the fact that it does not ferment mannite with the production of acid, and hence is sometimes called the "non-acid" or "alkaline" variety. Type I is claimed by Kruse¹⁹ to be the etiologic organism in true epidemic dysentery and he speaks of the organisms of Group B as "pseudo-dysenteric organisms." As the organisms of Group B have been isolated from cases of severe epidemic dysentery, this term has found but little acceptance. But it is quite generally conceded that, as a rule, the cases from which the Shiga organism has been isolated are clinically more severe and for this reason the term "para-dysentery" has been suggested and applied to Group B by Park,²⁰ Castellini²¹ and others. The toxins of the Shiga variety are partly soluble or exogenous, and those of the acid varieties are fixed in the organism or endogenous. As the toxins of the Shiga variety are far more toxic than those of the acid variety, the names "*giftigen*" and "*giftarmen*," respectively, are used by Lentz²² to distinguish the groups. According to Doerr no constant or characteristic toxin formed by the Flexner organism (Group B) has been found as far as animal experimentation has shown. A large part of the work on serum reactions — and this applies particularly to the studies on infants — is worthless because of the failure of early workers to distinguish between varieties. Each of the four types forms an homologous or chief agglutinin and at the same time heterologous or partial agglutinins for the other types. The serum distinctions are more marked between the acid and alkaline varieties than between the different members of Group B. According to Lentz²² the Flexner or "Y" variety may be agglutinated by the serum of a normal person in dilutions of from one-thirtieth to one-fiftieth, and hence partial agglutinins may be quite high. In artificial immunization partial agglutinins are formed for heterologous varieties which interfere considerably and which differ with the animals used. Thus the horse is not suitable for immunization with the varieties of Group B. The early technic for isolation of the organisms was laborious and possessed many difficulties and is one factor

19. Kruse: *Deutsch. med. Wchnschr.*, 1907, xxxiii, 292.

20. Park: *Jour. Infect. Dis.*, 1905, Suppl., 295; Park, Collins and Goodwin: *Jour. Med. Research*, 1904, xi, 551.

21. Castellini: *Jour. Hyg.*, 1904, iv, 495.

22. Lentz: In KÖlle u. Wassermann's *Hand.d.path. Microorg.*, 1909, Part 2, 391.

which has led to such marked differences in results. More recently the use of Endo's²³ medium which has been modified by Kendall and Walker²⁴ has come into use and this special medium has simplified the technic considerably.

In the summer of 1902 Duval and Bassett²⁵ undertook the study of infantile diarrheas at the Thomas Wilson Sanitarium in Baltimore with the purpose of determining the presence or absence of the dysentery organism. Positive results were reported in forty-two out of fifty-three cases, or approximately 80 per cent. Wide-spread interest followed this report as it was inclined to interpret their work as showing that "summer diarrhea" was an infectious process due to the *B. dysenteriae*. The following summer an extensive investigation was undertaken in Boston, New York, Philadelphia and Baltimore under the direction of the Rockefeller Institute.²⁵ In all 412 cases were studied, and of these 279, or 63.2 per cent., were reported as showing the presence of some type of the *B. dysenteriae*. The following table, which gives the results of the individual workers, shows that quite marked differences exist in their findings.

	No. of Cases	B. Dys. No.	Present Per cent.
Duval and Schorer	79	75	94
Bassett	73	51	70
Wollstein and Dewey	62	48	78
Cordes	51	26	51
Waite	47	19	40
Kendall	31	29	93.5
Lewis	21	11	52.5
Gay and Stanton Hospital	20	13	65
Gay and Stanton Tenements.....	28	7	25
	412	279	63.2

Examining more closely the tables of Duval and Schorer, who with Kendall report results which would lead one to believe that the organism was almost constantly present and the only organism of specific importance, we find that in twelve of the positive cases but one colony was obtained from an average of about sixteen plates. In only some twenty of their cases were a number of colonies isolated.

In addition to the Rockefeller investigations a number of independent studies have been reported. In the winter of 1902-1903 following Duval's and Bassett's first report, Wollstein²⁶ examined the stools from 114 cases of dysentery from the wards of the Babies' Hospital and Foundling Asylum in New York, and found the organism in thirty-nine cases, or 34 per cent. Wollstein does not give any idea as to the numerical presence of the organism.

23. Endo: Centralbl. f. Bakteriöl., 1904, xxxv, Orig., 109.

24. Kendall and Walker: Jour. Med. Research, 1910, xxiii, 481.

25. Studies from the Rockefeller Institute, 1904, ii.

26. Wollstein: Jour. Med. Research, 1903, x, ii.

In 1903, Dunn²⁷ examined sixty-one cases at the Infants' Hospital in Boston and reported thirteen positive cases, or 22 per cent.

Weaver, Tunnicliff, Heinemann and Michael²⁸ studied 102 cases in Chicago in the summer of 1904 and reported twenty-six, or 25 per cent., positive for the dysentery organisms. Twenty-four of the twenty-six cases were in children over 1 year of age. All of the organisms were of the "acid" variety, the "Flexner" occurring eleven times and the "Y" type forty-seven times. These colonies agglutinated most irregularly all four types of sera.

During the same summer an extensive investigation was made in Baltimore by Knox and Schorer,²⁹ the full reports of which have only recently been published. In all seventy-four cases were studied and in fifty-three, or 71.6 per cent., some type of dysentery bacillus was found. In seventeen, or 22 per cent., however, it was necessary to scrape the large bowel before obtaining positive results, and so the organism was only isolated from the stool in about 50 per cent. of the cases. Shiga organisms were found in fourteen cases, and in thirteen cases mixed infection occurred.

Lucas, Fitzgerald and Schorer³⁰ reported thirty-eight positive cases out of forty-five cases of "infectious diarrhea" at the Boston Floating Hospital in 1910.

In England, Morgan³¹ took up the study of summer diarrheas of infancy in 1905 and 1906. During the first summer Morgan examined the stools in fifty-eight cases of what he terms "acute infectious diarrhea," and twenty control cases. An organism which he calls *1 *Bacillus* was found in twenty-eight of the diarrheal cases and in only one of the controls. This organism was pathogenic for rabbits and monkeys and culturally resembled the hog cholera organism of MacFadyean. The following summer he found the same organism in nineteen of fifty-four cases of diarrhea studied. He reports that in none of the cases were true Shiga or Flexner organisms found. In 1910 Williams, Murry and Rundle³² encountered two organisms in thirty-three out of forty cases of "infectious diarrhea" in Liverpool. One, which they called *Bacillus* "F," is closely related to the paratyphoid organism, and the other they determined to be *B. suipestifer*. Stools from 100 normal school children were examined with negative results.

The French reports of bacteriologic studies of this subject go from one extreme to the other. For example, Auché and Campagna³³ report

27. Dunn: Am. Med.; 1904, vii, 737.

28. Weaver, Tunnicliff, Heinemann and Michael: Jour. Infect. Dis., 1905, ii, 70.

29. Knox and Schorer: Johns Hopkins Hosp. Rep., 1910, xv, 1.

30. Lucas, Fitzgerald and Schorer: Jour. Am. Med. Assn., 1910, liv, 441.

31. Morgan: Brit. Med. Jour., 1906, i, 908; 1907, ii, 17.

32. Williams, Murry and Rundle: Lancet, London, 1910, ii, 730.

33. Auché and Campagna: Arch. d. méd. d. enf., 1906, ix, 513.

thirty-three cases in which the "Shiga" variety was found fourteen times, the "Flexner" seventeen and the "Strong" seven times. On the other hand, Manicatide³⁴ examined fifty-four cases which were selected for their resemblance to true dysentery and was able to find the organism in but five cases, all of which were in children over 5 years of age. Forty-one cases under 1 year were negative. Dumas and Menard³⁵ were unable to find the organism in eight patients from whom blood cultures were taken.

The study of the stools of infants with diarrhea for the purpose of ascertaining the presence of dysentery organisms has received but little attention from German pediatricians who are inclined to attribute the pathologic conditions to chemical changes in the intestine and to altered metabolism. While admitting the possibility of infection by bacteria, they believe it to be a rare occurrence and of little importance. It may be emphasized, however, that the picture of infantile dysentery with blood in the stools, much mucus and occasional false membrane is a rare one in Germany. Charlton and Jehle³⁶ studied sixty cases in Vienna and found the Shiga type of dysentery bacillus nine times and the Flexner type thirteen times. The cases in which the Shiga type were found were clinically more severe than those in which the Flexner organisms were found, and the stools contained both blood and false membrane. For this reason they looked on the infection with the Flexner variety as secondary or terminal. Jehle³⁷ further reported nine cases in which the Flexner organisms were present, and found in these cases that blood-serum also agglutinated the colon bacillus. Leiner³⁸ reported several cases of infection with the Flexner organism in children from 2 to 6 years of age.

The most extensive study of the anatomic lesions in cases associated with the presence of the *B. dysenteriae* is that of Howland,³⁵ who reported the autopsy findings in thirty-two cases. In twenty-five of these cases the organism was recovered from the stools and in the remainder from scrapings of the mucosa at the autopsy. In five cases a pseudomembrane was present, which corresponds with one of the most frequent changes found in the epidemic dysentery of adults. Four cases showed a lymphoid hyperplasia with follicular ulceration, resembling the lesions described by Escherich¹⁰ as "follicular enteritis," and five cases showed a superficial ulceration of the mucosa not limited to the follicles. In far the larger group of cases—fourteen, or nearly one-half—few anatomic lesions were found, and none of any importance. This group of cases included a number of badly nourished and marantic infants and several cases of terminal infection. Knox²⁵ reported five cases with no distinctive or

34. Manicatide: Compt. rend. Soc. de biol., 1908, lxxv, 525.

35. Dumas and Menard: Compt. rend. Soc. de biol., 1907, lxxiii, 601.

36. Charlton and Jehle: Tr. Assn. Am. Phys., 1904, xix, 405.

37. Jehle: Munchen. Med. Wehnschr., 1906, liii, 101.

38. Leiner: Wien. klin. Wehnschr., 1904, xvii, 695.

characteristic lesions. More recently Knox and Schorer³⁹ reported a case (293) in which a diphtheritic membrane was present from which almost pure cultures of *B. dysenteriae* were obtained, but in another case (79) in the same report no dysentery organisms could be isolated from the pseudomembrane which was present. We have mentioned above the work of Charlton and Jehle³⁶ who found severe lesions associated with Shiga infections.

The organisms have never been recovered from the blood of an infant with ileocolitis despite the numerous attempts that have been made. By the use of the endomedium this has recently been accomplished in the case of an adult by Darling and Bates³⁹ and opens up a line of work which might be productive of some very important results.

A number of attempts have been made to isolate the organism from the stools of normal infants. Duval and Bassett²⁵ examined a series of twenty-five cases with negative results although later Duval²⁵ reported that he had found the Flexner organism in the stools of two normal infants. Wollstein²⁵ reported negative findings in thirty children, but found the organisms in the stools of three of twenty-four infants who died of other conditions. Charlton and Jehle³⁶ found the Flexner organism in two of ten patients examined. Collins⁴⁰ made a rather extensive study of fifty-six normal children. Three of these showed different types of the paradysentery group. She was unable to obtain the organism from the stool examinations in twenty-one cases of acute or subacute diarrhea. Kendall²⁵ recovered the dysentery organism in two cases of tuberculous enteritis, and Knox and Schorer²⁹ from a third case.

AUTHOR'S STUDY

During the summer of 1911 the opportunity presented itself to take up this question, which had not been studied to any extent since the introduction of media which permit of rapid and more accurate isolation of the dysentery organisms from the stools.

The material for the study consisted of eighty cases of acute intestinal disturbance, selected in large part from the Babies' Hospital of Philadelphia, and the remainder from St. Christopher's Hospital for Children. In addition, a number of cases from other sources were examined, but in the report we have confined ourselves to the eighty cases, which were all seen clinically by one of us (B. S. V.), and of which we have complete clinical, as well as bacteriologic records. The cases not on our own service were from the services of Drs. Sinclair, Judson and LeBoutillier at the Babies' Hospital, and Dr. Fife at St. Christopher's Hospital.

39. Darling and Bates: Am. Jour. Med. Sc., 1912, cxliii, 36.

40. Collins: Jour. Infect. Dis., 1905, ii, 620.

The cases were selected cases of a severe character and clinically were designated as ileocolitis. In every case mucus was more or less constantly present in the stools and frequently the stools were blood-streaked. It is in this type of case that the dysentery organisms have been most frequently found.

As regards age, 75 per cent. were between the ages of 3 and 8 months, inclusive. Only five were over 1 year of age. They may be roughly divided into two gross types: (1) those with acute attacks when in an apparently normal state of nutrition, and (2) those in whom there was an obvious chronic nutritional disturbance on which the acute attack was superimposed. The cases on this basis may be grouped, as regards their outcomes, as follows:

Acute cases	51	Acute on chronic 29
Cured	19	9
Removed improved	1	2
Removed unimproved	9	1
Died	22	17
Unfavorable result.....	50%	62%

We have used the word "cured" in the sense it usually appears in hospital reports. It would be far better to use the word "improved," as an investigation of patients "discharged as cured" from St. Christopher's and the Babies' hospitals the previous summer has shown that approximately 50 per cent. have died subsequently from a second acute attack, or from a chronic disturbance that has followed in the wake of the first acute attack.

It is of no advantage to go into the detailed histories of the cases. They represent a group of infants who had been acutely ill with diarrhea from one day to two or three weeks before admission (average one week) and who showed frequent mucus stools on admission, with blood present in about 20 per cent. Vomiting was frequently present on admission, and was practically never absent in the history. Fever was an irregular symptom, usually present on admission, falling in the majority of cases a few days later, when it became irregular. In most of the infants living over ten days there was a tendency toward subnormal temperatures. The feeding of the infant at the time of the acute onset is tabulated as follows:

Milk (market) (diluted or whole)	24
Condensed milk	25
Modified milk (pasteurized)	9
Breast fed	10
Patent foods	1
Oatmeal water	1
Table food	7
Unknown	3
	<hr/>
	80

The large number of infants who had been previously fed on condensed milk—a food rich in carbohydrate—is of interest in connection with Kendall's theories, which will be discussed later.

BACTERIOLOGIC EXAMINATION

The stools were collected in sterile anal tubes in the forenoon and taken directly to the laboratory where the various media were at once inoculated. One hundred and sixty-seven examinations of stools from the eighty patients were made, which were divided as follows:

No. of Cases	No. of Times Examined	Total	No. of Cases	No. of Times Examined	Total
40	1	40	1	8	8
18	2	36	4	6	24
12	3	36			
2	4	8	80		167
3	5	15			

Omitting the organisms constantly present in normal stools, and considering the bacteriologic findings as a whole, the results were as follows:

Organism	No. of Cases	Percentage
<i>B. dysenteriae</i> (acid)	18	22.5
<i>Streptococcus</i>	65	81.
Colon*	75	93.7
<i>Pyocyaneus</i>	24	30
The following combinations were encountered:		
Dysentery and colon		3
Dysentery and streptococcus		2
Dysentery and streptococcus and colon		13
Streptococcus and colon		50

The percentage of cases in which we found the dysentery organism is low in comparison with the majority of previous investigations. In our studies the enriching Endo-medium was used and hence but few plates were made from the stools, and it is possible that had a large number of plates been made, we would have occasionally encountered a colony of dysentery organisms in some of the cases reported as negative. In all of the cases the organisms were present in sufficient quantities to be considered as one of the predominating types of the intestinal flora. No attempt was made to subdivide the paradysentery organisms into their subvarieties, as this, as well as the serum reactions, have little if any practical importance in the light of previous studies.

Considering first the dysentery organisms the question arises as to the rôle played by them in the production of the acute intestinal diseases of infancy and early childhood. We have omitted from the paper a discussion of the clinical types of cases in which the organisms have been found. Although most frequently found in cases of ileocolitis, it is by no means confined to these cases, and has been isolated from very mild cases

* The colon organisms are enumerated because of their bearing on Kendall's studies, which are discussed in the latter portion of the paper.

of enteritis. A study of our own cases from the clinical standpoint failed to show any symptoms or combination of symptoms whereby it was possible to separate out the cases in which the dysentery bacilli were found. It has been quite definitely established that both the Shiga and Flexner types of dysentery organisms may produce dysentery, the former — in adults at least — being usually associated with a more severe clinical form, although this distinction is less clear in infants with their tendency toward gastro-intestinal disturbances. We find in infants a certain number of cases in which the stools contain large numbers of the dysentery bacilli and in some of which typical dysenteric lesions have been found at autopsy. Unfortunately we know little of the habits or method of transmission of this organism, but it has been found in the stools of apparently normal infants and in the stools of children suffering from other conditions. The earlier investigators with a few exceptions tended to blame a very large percentage of the severer intestinal cases on the dysentery organism, but a critical study shows that in a large number of their cases the organism was only occasionally found, and then with difficulty, and was of little numerical importance. The mere fact that an occasional dysentery organism is found in the stool of a case of enteritis is by no means proof that the organisms are the cause of the condition, and there is no evidence to show that in these cases the dysentery organisms have anything more than a casual relation. It seems to us that we have no right to group these cases together with those in which large numbers of dysentery bacilli are present and in which distinctive anatomical lesions are found in the fatal cases at autopsy. From a study of previous investigations and our own work we think that not more than 20 per cent. of the cases of ileocolitis may be attributed to the dysentery organisms and this figure may be high. The well known clinical fact that many of the mild cases of intestinal disturbance may pass into a severe form of ileocolitis raises the question as to whether we must consider the organism of primary or secondary importance. That is, whether a primary infection with the organism occur, producing the condition, or whether an invasion of the organism occurs after an intestinal disturbance has been produced in some manner not necessarily bacterial in nature. The answer to this is and must be merely a matter of opinion. We believe a comparatively small number are primary and that in the larger number of cases where the organism plays a rôle it is the form of a secondary invader. Our reasons for this are, first, that it has been found in all types of clinical cases and although more commonly found in ileocolitis it is typical of none; second, that in but few of the positive cases the characteristic and distinctive lesions of dysentery are found at autopsy, and third, that the organism has been found as a terminal infection in cases not primarily enteric in nature. Many objections may be raised against

this conclusion, but, as stated before, any view on this point is largely a matter of opinion.

Since the discovery of the dysentery bacillus there has been a tendency to relegate the streptococcus and other organisms to a place of secondary importance. Many of the earlier writers^{8, 9, 10} considered the streptococcus of primary etiologic importance, but the value of their observations was lessened with the discovery of the dysentery bacillus, as there is no means of knowing how many of their cases were in reality dysentery infections. But few of the investigations since have taken the streptococcus into consideration, as they have been chiefly concerned with determining the presence or absence of dysentery bacilli. As will be seen by our table, the streptococcus was present in some 80 per cent. of our cases—usually in association with other organisms. In some of the severe cases, however, almost pure cultures of streptococci were obtained from the stools and the dysentery organisms were not associated in these cases. Knox and Schorer²⁹ reported several cases in which the streptococcus was apparently at fault and Kendall⁴¹ has had a similar experience. While in by far the larger number of cases in which streptococci are found, the relationship is apparently nothing more than casual, in a certain number of cases it is probable that these organisms are of etiologic importance—cases in which distinct ulceration and false membrane are present in the intestine, and from which almost pure cultures of streptococci are obtained on bacteriologic examination. Too little work has been done on the other organisms, as *B. pyocyaneus*, to determine their exact importance although it does not seem probable that these, as the colon organism, are harmful in the intestinal tract.

SUMMARY

Our conclusions may be summarized at this point and are as follows:

1. The mere presence of a few dysentery organisms in a case of acute intestinal disturbance in an infant does not in itself prove that the organisms have any etiologic relation to the condition. It is only in the severe cases of ileocolitis that the dysentery organisms are present in the stools as one of the predominating types of organisms and it is these cases which show distinctive lesions of dysentery at autopsy.

2. In only about 20 per cent. of the cases of ileocolitis occurring in infancy are dysentery organisms found. While in some of these cases the infection with dysentery organisms is primary, in others it is probably secondary.

3. The cases of ileocolitis in which dysentery organisms are present cannot be separated clinically from those in which they are absent.

41. Kendall: Boston Med. and Surg. Jour., 1910, clxiii, 332; Boston Med. and Surg. Jour., 1910, clxiii, 398; Jour. Am. Med. Assn., 1911, lvi, 1084; Jour. Med. Research, 1911, xxv, 117.

4. Streptococci are present in the stools of about 80 per cent. of the cases of ileocolitis. While in the majority of these cases the relation is unimportant, it is probable that in some instances the organisms have a distinct relationship in the etiology of the condition.

Recently the study of the intestinal flora has been taken up by Kendall¹¹ from another view-point, namely, the "dynamic." Kendall has found that the intestinal flora of "bacillary dysentery"—a term which is loose and indefinite and which means clinically almost any type of diarrhea in its application to infants—consists of what he terms a "putrefactive group" of organisms. This is essentially a combination of *B. dysenteriae*, *B. coli* and the streptococcus. He has found by experiments *in vitro* that these organisms produce putrefactive decomposition of certain sugar-free media. If sugar is added to the media he finds that the production of fermentative substances inhibits the growth of the putrefactive types of organisms and the production of putrefactive substances. From this Kendall is led to advocate the use of a sugar solution—lactose—in the treatment of "bacillary dysentery" in order to inhibit putrefaction, and he claims to have observed the disappearance of a "putrefactive" flora and the development of a normal "fermentative" group of organisms (*B. bifidus* and *B. acidophilus*) under the influence of a sugar diet.

In connection with our studies we have followed the set of bacteriologic procedures which Kendall has employed in the examination of the stools and which is designed for the use of clinicians. They are, however, too elaborate to ever become of use to workers who have not had considerable laboratory experience and access to a well equipped bacteriologic laboratory, and in addition consume too much time to be of service to one engaged in clinical work. The method of study of each stool was as follows:

1. Study of types and numbers of bacteria in gram-stained fields of freshly-passed feces.
2. Type of reaction in milk heated to 80 C. (presence or absence of gas bacilli).
3. Study of gas volume, growth and sediments in dextrose and lactose fermentation tubes.
4. Character and amount of growth in acetic acid — dextrose broth.
5. Character of colonies developing in the modified "Endo-medium."
6. Character of growth in gelatin after three days at room temperature.
7. Plating of growths on litmus-mannite-agar for identification of the dysentery organism.

The gram-stained fields were negative in by far the larger number of cases. The number of organisms varied considerably, depending on

the fecal content of the stool. We cannot say that we learned much of value from a comparison of the gram-stained fields, nor did they serve as an index to the character of the individual case. At times negative and positive fields alternated without any apparent relation to the clinical conditions or diet.

Out of nearly 100 cases examined during the summer we found but one with the *Bacillus aerogenes capsulatus* and developing a growth in milk heated to 80 C. This child was placed on raw buttermilk, but died three days later and is not included among the eighty patients reported on.

The gas formation, growth and sediments in the dextrose and lactose fermentation tubes varied to such a marked degree in different cases showing the same types of predominating organisms and in individual cases without apparent relation to the clinical condition or changes, that in reality this part of the study gave very little useful information. The same was the case with the growth on and liquefaction of gelatin plates.

A few stool reports will show the degree of variation encountered:

Case	Predominating Organisms	Gas Formed in		Gram-fields
		Lactose, mm.	Dextrose, mm.	
J. G. Dysentery and colon		13	13	..
Ed. R. Dysentery, streptococcus and colon....		4	20	..
B. W. Dysentery, streptococcus.....		15	7	..
Est. C. Dysentery, streptococcus and colon....		14	31	..
J. W. Streptococcus and colon		19	20	..
H. B. Streptococcus and colon		6	2	..
L. B. Streptococcus and colon		9	1	..
Ida B. Streptococcus and colon		Tr.	15	..
Wm. B. Streptococcus and colon		23	17	..
J. B. (Lactose diet)—				
8-3 Streptococcus and colon		18	12	±
8-7 Streptococcus and colon		10	2	—
8-8 Colon and subtiloid		20	8	±

Unfavorable results in 58 per cent.

We found the modified Endo-medium most satisfactory for separating out the dysentery organisms in the stool and a distinct advance over previous methods.

In so far as the bacterial picture of ileocolitis consists to a large degree of some of the "putrefactive group" of organisms, i. e., combinations of *B. dysenteriae*, *B. coli* and the streptococcus, our findings were in accordance with those of Kendall. In thirty-one of the eighty cases a "lactose diet" was used despite certain theoretical objections, and the results were as follows:

Removed improved.....	1
Removed unimproved.....	4
Cured	12
Died	14
	<hr/>
	31

The results were much the same as in the whole series of eighty cases, but are too few in number to draw very definite conclusions. In those cases which were receiving lactose and improving, the "putrefactive" organisms gradually disappeared as the predominating types of organisms in the bacteriologic picture, while in those cases not improving they persisted. In other words, the disappearance was apparently dependent on the condition of the patient rather than on the diet.

While we have no argument as to the "*in vitro*" experiments of Kendall, several objections may be raised against his ideas as to the production of the acute intestinal diseases in infancy. According to his views the action of the "putrefactive group" of organisms is to produce putrefactive decomposition in the intestine and the products of this decomposition are the cause of the intestinal disturbance. So far as we know it has never been shown that the products of putrefactive decomposition arising from the action of *B. dysenteriae*, *B. coli* and the streptococcus produce the intestinal disturbance, and in this respect one of Kendall's chief premises is an assumption. Clinical evidence and experience go to show that in many instances the fermentative products are at fault, and that carbohydrates are more apt to produce trouble than any other single food element. The use of a food with a high protein content and with a low carbohydrate percentage is frequently followed by excellent results. If Kendall's treatment is to be used in those cases alone which show *B. dysenteriae* in the stools, it is of little value, as these cases cannot be separated clinically, and to wait until a stool examination has been made would be to waste considerable time which might in many cases determine the outcome of the case.

USE OF POLYCARBOHYDRATES IN THE DIET OF THE YOUNG INFANT *

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In recent times the rôle of the carbohydrates in infant feeding has received marked attention. Whether the importance they have assumed in the minds of some in the pathology of nutritional disturbances is justified must be decided by future study.

For years the adjustment of the carbohydrate percentage to the digestive and caloric requirements of the infant was considered the easiest part of the problem of infant feeding. The fact that mother's milk contains constantly 7 per cent. of lactose, furthermore the fact that lactose is of animal origin and is essentially the same whether human or derived from the cow, ass, rabbit, dog or horse, made this portion of the problem seem simple. To imitate Nature and furnish the infant with the same carbohydrate in the same percentage appeared to answer every requirement.

That lactose could cause digestive disturbances with the production of acid, green, foamy, watery stools as a result of fermentation has been recognized for many years. This disturbance was not considered of special frequency nor of great importance.

Many of our leading pediatricians hold lactose to be the ideal sugar for an infant; furthermore, the addition of a cereal to the diet of a young infant was not only considered unnecessary but actually harmful. For years it was believed that the young infant had little power of digesting starch, and, furthermore, the fact that the breast-fed baby thrived on a starchless diet strengthened them in this position. The early use of starches has been considered a frequent cause of intestinal indigestion; this disturbance frequently not manifesting itself until a later period of infancy. Still¹ believes that barley water in the milk mixture of a young infant plays an important rôle in the causation of rickets. He says "the addition of starch in any form to the diet of an infant under 8 months of age is liable to interfere with assimilation and in this way involves the danger of rickets, especially if the milk mixture is

*Read in the Section on Diseases of Children of the American Medical Association, at the Sixty-Third Annual Session, held at Atlantic City, June, 1912.

*From St. Ann's Infant Asylum and Pediatric Department, St. Louis University.

1. Still: Common Disorders and Diseases of Childhood, 1909.

already poor in fat." Holt² teaches that the average healthy infant is best nourished for the first four or five months on the elements of milk. He considers the addition of the various cereals to the milk of young infants as a useful measure for some, but not desirable for all. He states that the early use of much farinaceous food often results in serious harm. Roach³ in 1906 stated that starch should not form a part of the infant's food in the early months of the first year. Jacobi⁴ has for years persistently advocated barley as a diluent with the addition of cane sugar. While not overlooking the nutrient effect of the barley he believed the mechanical effect on the proteins was of great importance.

The work of Finkelstein and his pupils has caused the carbohydrates to receive the attention they deserve. That lactose may be the immediate cause of dangerous symptoms of intoxication in some infants, particularly if there has been an injury to the intestinal epithelium, is now admitted by many. Recently Leopold⁵ has advised a combination of dextrin and maltose in about equal parts as the best form of carbohydrates for the young infant.

Czerny⁶ selects milk-sugar for use during the first months of life and avoids the employment of other sugars or carbohydrates during the early weeks. Of lactose he adds 1 teaspoonful to each of five feedings in twenty-four hours. From the fourth month instead of increasing the amount of sugar he adds flour. He thinks by the early and systematic use of flour the danger of rickets and scrofula is not increased. He employs oat flour, wheat flour and cornstarch and considers them of more value than dextrinous flours. He believes the favorable influence of flour is due to the slow saccharification, which brings about a slow absorption of water, due to the sugar, which is more readily compensated for by the organism.

In a service of six years in one of the largest infant asylums of the West we have put into practice every possible method of infant feeding that has seemed justified. Mixtures of cow's milk and lactose, with the percentage of protein, fat and carbohydrate corresponding to the generally accepted principles of infant feeding have been employed innumerable times, but leave much to be desired. In recent times the results in our institution approach those obtained in private practice. Our results in the past compare very favorably with those reported by Mr. Homer Folks,⁷ secretary of the New York State Charities Aid Association, who in 1910

2. Holt: *Diseases of Infancy and Childhood*, 1911.

3. Rotch: *Pediatrics*, 1906.

4. Jacobi: *Therapeutics of Infancy and Childhood*, 1903.

5. Leopold: *Arch. Pediat.*, xxviii, No. 10, p. 844.

6. Czerny: *Des Kindes Ernährung, Ernährungs-Störung und Ernährungs-Therapie*, 1909.

7. Folks, H.: *Bull. Acad. Med.*, N. Y., February, 1910.

through the kindness of the Children's Department of the Russell Sage Foundation, investigated the mortality statistics of the infant asylums of the country. All of us recognize the difficulties under which we labor. The overcrowding, the lack of help and the frequency of epidemics all conspire to thwart our efforts. So great have the difficulties seemed that many have seriously considered the advisability of doing away with infant asylums. For many reasons such a course is not practical.

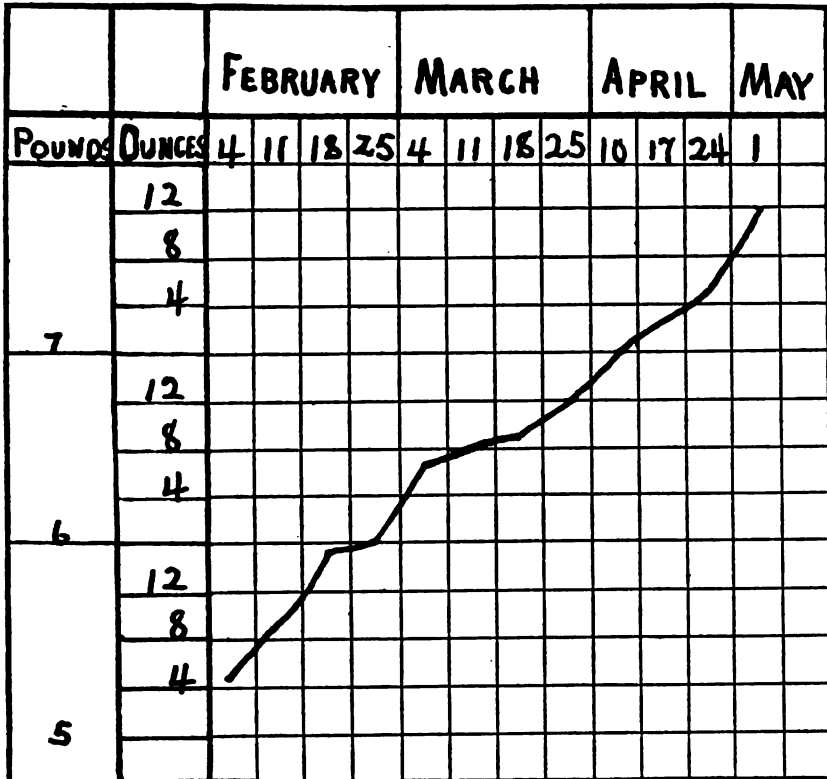


Chart showing weight curve of a much under-weight asylum infant receiving the polycarbohydrate diet.

The usual milk modifications employed so successfully in private practice do not give results in asylums. The asylum infant is a special problem, and in order to promote nutrition extraordinary measures must be resorted to. We have found that these infants are greatly assisted in battling with the surroundings by the use of a variety of easily assimilable carbohydrates. A high percentage of protein is fed even to the new-born infant and the percentage of fat is closely watched. Beginning with a fat-free diet at birth the percentage is gradually raised with the increase in weight of the baby. With the addition of fat to the mixture,

owing to its high heat value, the twenty-four-hour amount must be reduced so as not to exceed the caloric requirements of the infant.

MILK MIXTURE

One and one-half ounces by measure of barley flour is cooked with 16 ounces of water at least twenty minutes down to 10 ounces, and added to 20 ounces of skim sweet or acidified milk.* The latter we believe for many reasons is preferable in an institution. One-half ounce by measure of cane sugar and 1 ounce by measure of malted food containing dextrin and maltose are added. The carbohydrate content of the mixture would be represented by lactose 2.66, cane sugar 1.30, maltose and dextrin, 1.70, plus barley, 2.25, which is partly coextrinized. This gives a total carbohydrate percentage of 7.91. One liter has a caloric value of 415.

We have used this mixture over a period of eighteen months. Last July, owing to the favorable results, it was adopted as the routine formula for new-born infants. We do not wish to be understood as believing that the problem of infant feeding is going to be solved by one mixture that need never be varied. The individual infant will always furnish the indications for what is best for its metabolism. In an infant asylum, owing to the large number of babies and the scarcity of help, the best results will be obtained by minimizing the work and prescribing a few formulas which give the best results for the average infant. We are satisfied of the wisdom of supplying the young infant a liberal percentage of protein as represented in this mixture. This percentage we do not change throughout the first year; the same may be said in regard to this mixture of the various carbohydrates. The fat percentage demands a change from time to time; beginning with a fat-free diet, the percentage is gradually raised with the progress of the baby.

CLINICAL RESULTS

Over a period of eleven months this mixture was adopted as a routine formula in the ward for the young infants. One hundred and seventy babies were cared for; ninety babies received breast milk for the first two weeks of life, and then received this mixture. Forty-five received this mixture from birth; eighteen were between 2 and 3 months of age and seventeen, owing to nutritional disturbances, were on *Eiweissmilch*; these received this mixture after completion of the *Eiweissmilch* cure. During this period there was a remarkable absence of babies with nutritional disturbances; the stools were uniformly of good color and consistency. No infant on this mixture in this series developed the symptom-complex described by Finkelstein under the caption alimentary intoxication,⁹ nor did symptoms arise which could be interpreted as *Mehlnahrungsschaden* (starch injury) in the sense of Czerny and Keller. Twelve babies did not show a satisfactory gain, so they were transferred to

8. Brady, J. M.: Arch. Pediat., 1910, xxvii, No. 6.

9. Finkelstein, H.: Jahrb. f. Kinderh., January, 1907, p. 1.

Eiweissmilch. All the other babies thrive satisfactorily, the fat percentage alone requiring alteration. Eighteen babies died, a mortality of 10.5 per cent. The causes of deaths were as follows: two sudden deaths, nutrition good; autopsy showed enlarged thymus; one, premature birth; one, congenital syphilis; seven, acute bronchopneumonia, nutrition good; one, phlegmon of the scalp; and six, decomposition (Finkelstein).

It will be seen from the above that 170 babies all under 3 months of age were cared for with only six deaths from nutritional disturbances. It is the experience of all that the great difficulty in an asylum is in establishing the nutrition of the infants. In passing it is to be remarked that while it is the desire to show the favorable results of this polycarbohydrate diet, it must be emphasized that the use of *Eiweissmilch* has prevented the deaths of a number of babies. The routine adoption of this diet for the young infants has limited very much the use of *Eiweissmilch*. Our infants remained under observation for variable periods ranging from one to six months; the large majority for a longer time than three months. I recall that the death-rate during the first year in private homes is generally stated to be 20 per cent.; Cautley says infant mortality is very high in the first month, sinking to less than half in the second month, and progressively decreasing with each successive month during the first year.

Statistics frequently deceive and therefore I believe just as much value may be placed on the impressions of the observer; I therefore offer the above figures for what they are worth.

DISCUSSION

In the past we have erred by feeding too much fat and too little protein and have condemned the use of cereals. The typhoid fever patient of to-day is assisted through his illness by a more liberal use of food-stuffs; likewise, the asylum baby can only withstand the results to which it is subjected by a liberal diet. Formerly we believed that the young infant could not digest starch; that it did not thrive owing to the fact that the digestive organs were not properly developed. Now we know that the new-born infant is abundantly supplied with all the digestive ferments. Diastatic ferment is found in the parotid gland as early as the fourth month of fetal life. There is no dearth in the supply of lactase, maltase, saccharase and amylolytic ferments in the infantile alimentary tract; therefore the ability to care for a variety of carbohydrates. Why the metabolic processes are favored, leading to an increased storage of salts and water in the tissues, is not apparent, but clinical results prove this. The very best indication that an infant is thriving is the presence of a regular gain in weight; if this does not occur the clinician cannot remain passive; something must be done. A sudden increase of weight

such as accompanies the development of edema, due to a pathologic state of the endothelial cells lining the capillaries, should not be misinterpreted. Use of these various carbohydrates in the dietary of the young infant with the careful exhibition of the fats seem to have a strong influence in maintaining the normal salt balance which we now recognize is a *sine qua non* in the metabolism of the healthy infant.

That the nutrition of an infant is favorably influenced by the use of more than one carbohydrate has been emphasized by Keller⁸ and Czerny, who speak of the use of two carbohydrates, either wheat flour and cane sugar, or wheat flour and maltose, in case of disturbed nutrition.

Striking results have been met with in infants in private practice who have failed to thrive and have lost weight. It is a mixture well adapted to follow up a malt soup¹⁰ or *Eiweissmilch* cure.

It has been determined that normally 90 per cent. of the heat requirements of the infantile organism are furnished by the sugars and fats; for a time a deficiency of the one may be compensated for by an increase of the other without ill effects. That fat in the diet of some, particularly the marantic and asylum infant, tends to have a *decomponirend* action, makes it advisable in the early weeks to allow the carbohydrates to furnish the energy usually supplied by the fats until the weight has started upward. This one-sided diet for well-known reasons must not be continued over too protracted a period.

Metabolism experiments show that the protein in the diet of the normal infant should supply not more than 10 per cent. of the total energy in the food. These experiments indicate that when these figures are exceeded there is danger of its specific dynamic action, whereby the total heat production of the body is markedly elevated. Not only does this lead to fever, but the digestive tract is enormously taxed, likewise the kidneys. That the intermediary metabolism is unfavorably influenced is also claimed.

One liter of the above mixture contains 23.11 gm. of protein, which, multiplied by 4.1, the heat value of 1 gm., equals 94.75 calories. To cover its caloric requirements an infant weighing 8 pounds and 13 ounces would require 1 liter equaling an energy quotient of 100. In this diet the protein would furnish the infant 22.83 per cent. of the total energy of the mixture. Theoretically for the above-mentioned reasons this would be very undesirable. Practically, for the asylum infant and the marantic infant in private practice, it does not apply. These infants thrive on this high protein diet in association with the liberal use of the various carbohydrates. Any unfavorable effect from the proteins exerting their specific dynamic action is not apparent clinically. We have repeatedly attempted to advance the nutrition of our infants by feeding a protein

10. Brady, J.: Jour. Am. Med. Assn., March 16, 1912.

percentage which would not furnish more than 10 per cent. of the total energy of the food. Results far superior were obtained with the percentage indicated.

That the above statement that the proteins should not furnish more than 10 per cent. of the total energy of the food does not hold in practice for the run-down infant is shown by the results obtained by feeding *Eiweissmilch*, 1 liter of which without the addition of sugar contains 417 calories; 4 per cent. addition of a malted food raises the caloric value to 550. The mixture contains 30 gm. of protein to the liter which, multiplied by 4.1, yields a caloric value of 123. This would mean that the protein in *Eiweissmilch* as usually fed would represent 22.36 per cent. of the total energy in the food.

Metabolism experiments indicate that flour in the diet such as barley causes an increased retention and utilization of nitrogen; protein is stored in the body with a resulting increase in weight and growth.

RICKETS

The greatest objection will be raised by those who see a close relationship between starch in the diet and rickets. This belief is founded on clinical observations. The cause of rickets is unknown and according to Zappert¹¹ of Vienna no more is known to-day about the nature of this disease than was known fifty years ago. That diet must play an important rôle in its causation is shown by the scarcity of severe forms of the disease amongst the breast-fed.

When we see in an asylum infant after infant fed on milk diluted with water with the addition of milk-sugar, fail little by little until at 6 weeks or 2 months of age it remains but a shadow of itself, while on the other hand we visit a ward of seventy infants and find the large majority of these infants making regular weekly gains, who would not declare for the diet of the latter no matter how much at variance it seems to be with the natural food?

If we consider the prominences of the epiphyseal boundary of the ribs with flexibility of the cranial bones at the margin of the sutures evidence of rickets, then 80 per cent. of our infants will show the disease. But that many of our infants show the condition in a severe form we cannot admit. Kassowitz of Vienna, Epstein of Prague and Kissel of Moscow calculate that 89 to 90 per cent. of the children of their out-patient clinic are rachitic. Then again, there are authorities such as Fischl, of Munich, who among others found only 5 per cent. of their clinical material rachitic. The difference in these figures must be due to the variations in views in regard to what is sufficient to establish the diagnosis.

11. Jacobi: *Dis. of Child.*, 1911, p. 237.

CONCLUSIONS

1. Mixtures of milk, water and lactose with fat, protein and carbohydrate in the percentage corresponding to the widely accepted principles of infant feeding do not give satisfactory results in an infant asylum.

2. The asylum infant, even in the early weeks, is greatly assisted in making gains and weathering the unfavorable surroundings by a liberal use of barley, maltose, dextrin and cane-sugar in the diet.

3. The exhibition of polycarbohydrates in the diet is an excellent therapeutic agent for the infant in private practice who refuses to gain on the usual milk mixtures or has already run down on the same.

4. For this diet to be successful the protein must be liberal in amount and special attention must be paid to the fat, which should only be raised with the increase of the weight of the baby.

5. The fear of rickets need not be considered; the first requirement is that the infant be kept alive. "*Probiren geht über studiren.*" Practical experience overrides theoretical conclusions.

APPENDICITIS IN CHILDHOOD

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There have been cared for in the first surgical service at the German Hospital of Brooklyn (1900-1912) 183 patients with appendicitis under the age of 12 years. Two patients, moribund on admission, were not operated on and died. In two interval cases the patients were operated on and recovered. The remaining 179 were acute cases in which the patients were operated on, of whom twenty died.

Proportion of Children to Adult Cases.—The total number of cases during the same period was 1,115, the proportion of children (183) 16.41 per cent.

The present report is founded on the last hundred consecutive personal operations for acute appendicitis in patients under 12 years of age.

Mortality.—Three of these patients died in the hospital; one patient with abscess died months later following resection of the intestine for tuberculosis and obstruction. Two of the three deaths from operation were in diffuse septic peritonitis cases, the other in a case in which a very acutely inflamed appendix with a perforation, operated on in less than twenty-four hours, and with an escaped enterolith which lay post-cecal directly on the iliac vein. This patient died in forty-eight hours of septicemia in spite of vaccine therapy and supportive measures. The operative mortality was 3 per cent.; the disease mortality 4 per cent. There has been but one death in the last fifty-six cases. (In the last hundred personal operations for acute appendicitis in adults six died.)

Age.—The youngest patient was 2 years and 9 months old; the oldest 12 years.

Age, Years.	No. of Cases.	Age, Years.	No. of Cases.
11-12	19	6-7	9
10-11	18	5-6	5
9-10	13	4-5	6
8-9	14	3-4	2
7-8	13	2-3	1

Sex.—Sixty-three were males; thirty-seven females.

Previous Attacks.—Eleven gave a history of one previous attack; four had two previous attacks; two had three previous attacks; one had four previous attacks; eighty-two patients were operated on in the first attack.

Duration of Attack.—Nineteen were operated on in the first twenty-four hours; thirty-three in the second twenty-four hours; twelve in the third; twenty-one in the fourth; four in the fifth; seven on the seventh day; four after two weeks.

Blood Examination.—In seventy cases the examination of the blood was recorded. The average leukocyte count was 19,106; the average polynuclear, 79.7 per cent. The highest leukocyte count was 48,200; the lowest, 8,200; the highest polynuclear, 92 per cent.; the lowest, 63 per cent.

Condition Found at Operation.—Inflammation limited to the appendix (in this class are included cases of all degrees of severity of inflammation, perforation and gangrene, so long as there is but slight involvement of the peritoneum in the neighborhood), thirty-six cases; with localized abscess, twenty-one cases; with abscess and spreading peritonitis, two cases; spreading peritonitis without abscess, eight cases; with diffuse septic peritonitis, thirty-two cases; with localized peritonitis, one case.

Cause of Death.—Two of the deaths could have been prevented by early diagnosis; two deaths were not preventable; in one there was sepsis from the appendix directly entering the circulation through the medium of the iliac vein; in the other the patient died two and a half months after the original operation as a result of a resection operation for tuberculosis with intestinal obstruction.

Operative Technic.—The appendix is larger in proportion to the rest of the intestine in childhood, while the mesentery of the appendix is not apt to be so well developed as in adult life. Removal of the appendix in all cases with as little disturbance of the neighboring intestine as possible; wick drainage if necrosis is present in the neighborhood of the appendix; glass tube drainage of the pelvis for diffuse peritonitis; wound closure except for the emergence of the drain. Vaccine therapy in septic cases.

Postoperative Treatment.—Rest in bed. Fluids 2 to 4 ounces every two hours and saline by rectum for the first twenty-four hours if no peritonitis is present. Murphy proctoclysis in all cases deprived of fluids. Deprivation of fluids by mouth if peritonitis is present until normal wound temperature is reached; elevation of the head and trunk in all peritonitis cases to lessen the rapidity of absorption; enema daily and as frequently as necessary to control distention; gastric lavage if stomach is distended.

Complications.—The complications are the same as in adults. Diffuse septic peritonitis occurs more readily in children as the omentum is thin and poorly developed and for this reason cannot afford the efficient barrier to spreading inflammation so often observed in the adult. Sec-

ondary abscesses are more common with diffuse septic peritonitis in children.

Dilatation of the Stomach.—Dilatation of the stomach from excessive fluids occurs more frequently in children than in adults. It is early and easily recognized if frequent palpation of the upper abdomen is made a routine, and quickly remedied by lavage and restricted fluids.

Diagnosis.—Nothing shows so well the advance in the diagnosis of appendicitis as a comparison of the number of cases occurring in children diagnosed during the first decade in the history of appendicitis, and the number in which the diagnosis is now made. From 1887 to 1897 at the Methodist Episcopal Hospital of Brooklyn (Drs. George R. Fowler and Lewis S. Pilcher, surgeons) there were treated 340 patients with appendicitis, of whom but twelve were under the age of 10 years; thus $3\frac{9}{17}$ per cent. of all cases were in children. It is noteworthy that not a single female child was treated for appendicitis in this series.

From 1900 to 1912, 1,115 patients were treated in the first surgical service at the German Hospital of Brooklyn, of which number ninety-two were under the age of 10. A comparison of these figures speaks well for the progress made by the general practitioner in diagnosis.

The History of the Case.—I am impressed with the belief that the diagnosis of appendicitis can be made in the majority of cases with a fair degree of certainty before the disease has advanced sufficiently to cause pain in the right iliac fossa. The early symptoms are sudden, gradually increasing pain, not necessarily severe, in the epigastrium or about the umbilicus, with some diffuse abdominal pain not accompanied by tenderness. If food has recently been partaken of, the stomach is emptied by vomiting. The symptoms persist for a few hours, then disappear not to return for a variable length of time. These symptoms recurring from time to time in a child and not directly assignable to other causes are the early symptoms of appendicitis. I have operated soon after these symptoms and found indubitable evidence of recent inflammation of the appendix. Usually the history is practically the same as in adults, with this exception, that whereas the average adult with an attack of cramps which later localizes in the right iliac fossa will keep quiet and permit the inflammation to localize or subside, children will be up and about as soon as the severe pain has passed.

Overfeeding and ill-advised feeding are so common in children that this factor must always be considered. It is quite frequent to get a history of extraordinary indiscretion and no doubt this acts as a causative factor in the production of the disease. If the eyes are dull and the child listless with a fever out of proportion to the abdominal symptoms, intestinal indigestion should be considered. In any event a blood examination will be of material aid. The factor of possible "indigestion" is apt to

cause delay, as the parents usually give the child a laxative when the pain is first complained of. This may result in a spread of the inflammation.

Usual History.—The child is taken suddenly ill with pain in the abdomen and coincident vomiting; a cathartic is given, following the action of which the patient is relieved and plays about, though occasionally complaining of cramping pain. The pain continuing a physician is summoned during the first twenty-four hours if the parents are intelligent, otherwise later. The diagnosis can be made in the first twenty-four hours on this history plus localized rigidity at any part of the abdomen. Fever may be absent or there will be slight fever, 100.5 and very slight, if any, acceleration of pulse, 90 to 100. In more severe cases the above symptoms are present in an exaggerated form and there is added painful distention and diffuse abdominal tenderness (spreading peritonitis).

A history of previous attacks is of value if classical; i. e., diffuse abdominal pain or pain about the navel or with subsequent localization at any point. It is also of value even though there is no history of localization if indiscretion in diet can be ruled out.

Temperature and pulse are of hardly any value in diagnosis except that a high temperature early in the case would rather cause one to suspect some lesion (pneumonia) other than appendicitis. Quite often the abdomen is opened in a patient with a temperature of 100 F. and a gangrenous condition of the appendix is disclosed. Taken in connection with other symptoms the temperature and pulse may be of some value in determining how the patient is combating the infection, but a low temperature must not lead to a sense of safety.

Vomiting is a common symptom but present in many of the diseases of childhood. It is of value when there is a history of several attacks of vomiting with diffuse pain or pains at the navel, without any indiscretion in diet.

Condition of the Bowels.—Usually the bowels have been moved by a cathartic before a physician is called. This practice should be discouraged as it tends to spread any existing inflammation and may transform a case with early perforation and localized peritonitis into a diffuse septic peritonitis.

The bowels are usually *constipated* at the beginning of the attack. The constipation has usually not existed for more than twenty-four hours, and there is slight distention. This distention is responsible for some of the pain, which latter is much relieved following a successful enema and the passage of gas. Paresis is a rare complication in children. If present there is *absence* of *peristalsis*. This is the differentiating symptom between paresis and mechanical obstruction and obstruction from localized peritonitis.

Diarrhea may occur but is rare. If there are blood-stained, small, repeated movements with straining, intussusception is probable.

Abdominal Examination.—In the majority of cases the diagnosis can be made by the abdominal examination, irrespective of the history. In making the examination the hands should first be warmed to avoid any abdominal reflex from cold. Tact and gentleness are necessary. If possible the confidence of the child should be secured; if not, the attention should be distracted. The posture of the patient is not of significance unless he lies on his back with the knees drawn up and recurs to that position when permitted, or when slight pressure is made over the appendix. Such a position indicates early in the disease that the appendix lies in the neighborhood of the anterior abdominal wall; later in the disease, that there is abscess formation along the iliac-psoas muscle. The patient may lie on the left side with the knees drawn up, not necessarily because there is great pain but because this is the easiest posture to assume.

For examination the patient is placed on the back, the abdomen, thighs and chest exposed and the limbs drawn down. Inspection will reveal the condition of the intestinal tract, whether distended or not, and in thin patients the presence or absence of peristaltic movements, the type of respiration, and in some instances the presence of a tumor. Respiration in young children is normally of the abdominal type; therefore if the abdominal muscles are held rigid and the costal type of respiration be present, a painful abdominal condition or a pulmonary condition will be suspected. The respiratory rate, unless excessive, is not of much value as it may be due to distention from any cause. While palpating the abdomen it is best to watch the child's face and to indulge in such conversation as will tend to distract the attention, not alone for this reason but also because a child's face is the mirror of his feelings and one can detect pain or tenderness there as the fingers gently palpate the abdomen. If successful in distracting the attention, palpation is easy, though true muscular rigidity will be harder to obtain than tumor.

Local muscular rigidity is easier to elicit than general. It is at times difficult to say whether general rigidity is voluntary or not. General rigidity may also be present in pneumonia and diaphragmatic pleurisy. Real rigidity is absent if the appendix is in the pelvis.

Tenderness is difficult to elicit as the child does not easily differentiate between pain and tenderness. Fear must be overcome to be certain.

Tumor is present or absent according to the period of the attack. In slowly progressive cases a tumor is formed in the second twenty-four hours. In mild cases and in rapidly progressive cases (cases of early perforation) there is no tumor. The advent of a tumor should not be awaited.

The loin is also palpated, as in quite a few cases the appendix is retrocecal and to the external side of the colon so that abdominal rigidity is lacking while present in the loin. In non-descent of the cecum the rigidity and tenderness is at the level of or even above the umbilicus. The appendix may stretch across the abdomen and be inflamed at the tip so that the inflammatory symptoms are then on the left side. Failure to discover rigidity and tenderness in the abdomen or loin does not rule out appendicitis, for the appendix may lie in the pelvis, in which event a rectal examination is essential.

Rectal Examination.—Delatour in 1898 called attention to the value of rectal examination in doubtful cases.¹

Rectal examination is particularly valuable in children for the examining finger reaches much further than is the case in an adult. Its routine employment would lead to earlier diagnosis in a considerable proportion of cases, while in some cases in which the appendix lies in the true pelvis it is only per rectum that the enlarged appendix or abscess can be felt.

Anesthesia as an Aid to Diagnosis.—The abdomen of a child, owing to the thinner abdominal walls and more shallow pelvis, is much easier to palpate, having gained the child's confidence, than the abdomen of an adult. In doubtful cases, having excluded pulmonary disease and exhausted other means, an anesthetic may be administered and the abdomen palpated. I have never found this necessary, but can imagine that in certain cases it would be of value. Under anesthesia it is easy in children, except in cases with extreme distention, though not always desirable for fear of rupturing adhesions, to palpate the appendix.

Should anesthesia be used for purposes of diagnosis it would be well to have everything ready for immediate operation.

Diagnosis of Unusual Cases.—At times the diagnosis is very difficult. There are cases in which the appendix lies in the pelvis and in which the infection is pure colon bacillus. In such cases the exciting cause seems to be a marked indiscretion in diet. A physician is called to attend a child who has vomited indigestible material, for instance, a last year's candy Easter egg or a breakfast of discarded bananas, as in two of my cases, and the vomiting is frequently repeated. There is diffuse abdominal pain, distention, no rigidity, slight diffuse tenderness. The patient vomits and has diarrhea. There is slight fever sometimes or none at all. The natural diagnosis in such instances is gastro-intestinal irritation from indigestible food and the treatment usually followed is a course of calomel followed by magnesia and starvation. The bowels move, the diffuse abdominal pain disappears and the child is kept in bed for a few days. Apparently

1. Delatour: Brooklyn Med. Jour., November, 1898.

all is well when suddenly the temperature rises, there is pain in the lower abdomen and an examination shows rigidity in the lower part of the abdominal wall. It is then that the diagnosis of appendicitis is first thought of. Operation discloses an abscess in the pelvis surrounding the appendix and a condition of spreading peritonitis. Such patients usually recover though the convalescence is much prolonged and is apt to be accompanied by secondary abscess formation. In these cases an early digital exploration of the rectum would have disclosed the condition. The explanation of such cases lies in the location of the appendix and the fact that the infection is a pure colon one.

Differential Diagnosis.—Many patients are referred to the surgeon for operation for appendicitis who have not appendicitis. Some of these patients have no surgical lesion at all and are cases of pneumonia, typhoid fever, menstruation, distended bladder, fecal impaction or errors in digestion; others have surgical lesions not demanding operation, as hip-joint disease; while still others, and these are in the majority, have intussusception or other form of intestinal obstruction, abdominal tumor, tuberculous peritonitis or torsion of the ovary.

It behooves the operator to be exceedingly careful in his diagnostic methods or he will have the mortification of operating unnecessarily. A blood examination should be made whenever there is any doubt as to the diagnosis. It will rule out certain lesions with certainty. The blood count in children does not offer any peculiarities.

In typhoid fever if there is doubt the blood examination will show whether there is typhoid fever alone, or whether, as is true in a small proportion of cases, there is also an appendicitis.

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PROGRESS IN PEDIATRICS

INFANT FEEDING AND DISORDERS OF THE DIGESTIVE SYSTEM

RÉSUMÉ OF THE LITERATURE OF THE PAST SIX MONTHS

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PHILADELPHIA

INFANT FEEDING

Breast Feeding.—Everybody will agree with Hunt¹ that no one has ever composed a substance which can replace human milk for the well baby. During the two weeks after birth Jaschke² gave breast milk only to 100 institution infants. If a mother was ill or had not enough milk, another mother nursed the infant in addition to her own baby. Eighty-one gained in weight regularly. Jaschke believes that, where nursing mothers are always to be had, every infant can be breast fed successfully. Rietschel³ fed seventy-three infants on the breast solely during the first six weeks of life. He allows but six feedings in twenty-four hours, rarely seven or even eight. Laurentius,⁴ who studied twenty-one wet-nurses, found that, when one mother nurses several infants, her milk-supply is enormously increased. Helbich⁵ secured similar results with the regular use of the breast-pump in ten women.

That breast milk is not always an ideal food for sick babies has been shown by Langstein and Hörde,⁶ who pumped out the breasts and gave the milk to 188 institution infants, twenty-nine of whom died (15 per cent.); 111 recovered (59 per cent.), while forty-eight showed no improvement (26 per cent.). They advise pumping out the breasts and giving the milk to the baby during the first days of life, so that both breasts are emptied regularly and the baby receives enough food without too great exertion. On the other hand, Wieland⁷ and Variot and Morancé⁸ consider that breast milk is of therapeutic value in the nutritional disturbances of infancy. Strathy⁹ states that the breast-fed baby

1. Hunt, R. B.: Boston Med. and Surg. Jour., 1912, clxvi, 367.
2. Jaschke, R. T.: Monatschr. f. Geburtsh. u. Gynäkol., 1912, xxxv, 60.
3. Rietschel, Hans: Jahrb. f. Kinderh., 1912, lxxv, 403.
4. Laurentius, Johannes: Arch. f. Kinderh., 1911, lvi, 275.
5. Helbich, H.: Monatschr. f. Kinderh., 1912, x, 311.
6. Langstein, L., and Hörde, E.: Therap. Monatsh., 1911, No. 12.
7. Wieland, Emil: Cor.-Bl. f. Schweiz. Aerzte, 1912, xlii, 149.
8. Variot and Morancé: Bull. Soc. de pédiat. de Paris, 1912, xiv, 120.
9. Strathy, G. S.: Canadian Practitioner and Review, 1912, xxxvii, 76.

is brought to the physician only because of failure to gain in weight or for colic. For the former he advises rest, exercise and correct food for the mother; for the colic he orders regular feedings at longer intervals and also reduces the time of each feeding. Lavage may be of benefit. Until such attempts have failed the baby should never be weaned; then he begins with mixed feeding.

The importance of breast feeding is the main theme of articles by Elliott,¹⁰ Spriggs,¹¹ Hale,¹² Mills¹³ and Labbe.¹⁴ Davis¹⁵ points out its value in the prevention of infantile mortality. He found that 72 per cent. of 736 babies born in Boston were breast fed. Howard¹⁶ tells how, in the milk stations of the Boston Milk and Baby Hygiene Association, one-third to one-half of all infants are breast-fed, partially or entirely. This supervision has materially lengthened the period of breast feeding.

That infants who have been weaned may again be put back on the breast with success has been shown by Wile,¹⁷ who reports six infants nursed again ten days to two months after weaning. Supplemental feeding may be necessary for a month after replacing the baby on the breast. After a contagious disease or breast abscess efforts should be made to get the baby back to the breast. In the case of puny infants an older, stronger child should be put to the mother's breasts to develop a supply. Mayerhofer¹⁸ reports several similar cases.

Meigs and Marsh¹⁹ have made a series of analyses of human milk which confirm Meigs' earlier work. The protein is about 1 per cent. and very slight changes occur during lactation. Friedenthal²⁰ discusses the important rôle played by the salts of human milk in the feeding of infants. Dibbelt²¹ draws attention to a physiologic lack of lime salts in human milk when the infant is about 7 months old. This may be a cause of rachitis. That milk from an eclamptic mother should not be given the baby is Frost's²² conclusion, as three died of the four infants whose mothers nursed them after convulsions. Davis²³ agrees with him,

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10. Elliott, T. H.: *West Virginia Med. Jour.* 1912, vi, 378.
 11. Spriggs, E. I.: *Clin. Jour.*, 1911, xxxix, 33.
 12. Hale, S. E.: *Southern Med. Jour.*, 1911, iv, 821.
 13. Mills, A. E.: *Australian Med. Jour.*, 1912, ii, 428.
 14. Labbe, E. J.: *Northwest Med.*, 1911, iii, 312.
 15. Davis, W. H.: *Boston Med. and Surg. Jour.*, 1912, clxvi, 242; and *Am. Jour. Pub. Health*, 1912, No. 2, p. 67.
 16. Howard, A. E.: *Boston Med. and Surg. Jour.*, 1912, clxvi, 773.
 17. Wile, I. S.: *Jour. Am. Med. Assn.*, 1912, lviii, 775.
 18. Mayerhofer, E.: *Wien. klin. Wehnschr.*, 1912, xxv, 272.
 19. Meigs, A. V., and Marsh, H. L.: *Med. Rec.*, New York, 1911, lxxx, 1300.
 20. Friedenthal, H.: *München. med. Wehnschr.*, 1911, lviii, 2411.
 21. Dibbelt, W.: *Berl. klin. Wehnschr.*, 1911, xlviii, 2058.
 22. Frost, C. A.: *Arch. Pediat.*, 1912, xxix, 55.
 23. Davis, E. V.: *Jour. Am. Med. Assn.*, 1912, lviii, 1676.

believing that the mother's toxemia may cause the death of the baby as late as three weeks after birth.

Breast milk is also of value for premature infants. Samuelson²⁴ concludes that the energy quotient for premature infants should be from 115 to 150. Hess²⁵ advises breast milk for premature infants, diluted with water or sugar water, with a caloric value of 30 the first day and increases the food 10 calories daily. If indigestion develops, the food value is kept at about 90 calories a day. At two weeks a baby weighing under 1,500 gm. should take 120 to 140 calories; one weighing over 1,500 gm. 110 to 130 calories. Artificial heat is always necessary; also one-eighth of the body weight of water should be given in twenty-four hours. Failure to gain and indigestion were noted when 140 calories per day was exceeded.

Mayerhofer and Pribram²⁶ report 100 infants fed successfully on breast milk preserved by the addition of hydrogen peroxid and calcium dioxid.

ARTIFICIAL FEEDING

Certified Milk.—That certified milk is the best form of cow's milk an infant can obtain is not to be denied (Porter,²⁷ Mosher,²⁸ Rice²⁹). Labbe,¹⁴ who is strongly in favor of breast feeding, notes that accidents may happen even with clean cow's milk. Delépine³⁰ says that, though infantile mortality is still high in Manchester (England), the reduction of the amount of tuberculous milk supplied to the city has had a distinctly beneficial effect on infant mortality, which has been markedly reduced in the last twenty years.

Methods.—While most writers (Darling³¹) still advocate percentage feeding, checked by calculation of the caloric value of the day's feedings, Abt³² and Chapman³³ prefer simple milk dilutions. Abt³² gets satisfactory results on milk diluted with water or a cereal, with 1 to 5 per cent. of sugar added. Elaborate and complicated formulas are not required. The careful preparation and proper administration of the food are not the least important elements in successful feeding. Chapman³³ prefers diluted whole milk. While the advantage of percentage feeding is accuracy, the main disadvantage is its difficulty of application. Levy³⁴

24. Samuelson, S.: *Ztschr. f. Kinderh.*, 1911, ii, 18.

25. Hess, J. H.: *AM. JOUR. DIS. CHILD.*, 1911, ii, 302.

26. Mayerhofer, E., and Pribram, E.: *Ztschr. f. Kinderh.*, 1912, iii, 525.

27. Porter, Langley: *Cal. State Jour. Med.*, 1911, ix, 415, and 460.

28. Mosher, G. C.: *Dietet. and Hyg. Gaz.*, 1912, xxviii, 137.

29. Rice, C. H.: *New Orleans Med. and Surg. Jour.*, 1911, lxiv, 370.

30. Delépine, Sheridan: *Lancet*, London, 1912, i, 1424.

31. Darling, E. A.: *Boston Med. and Surg. Jour.*, 1911, clxv, 747.

32. Abt, I. A.: *Chicago Med. Rec.*, 1912, xxxiv, 115.

33. Chapman, W. D.: *Illinois Med. Jour.*, 1912, xxi, 580.

34. Levy, David: *Jour. Am. Med. Assn.*, 1912, lviii, 1925.

gives one-half milk up to 6 months, two-thirds milk to 9 months and then undiluted milk. He allows five feedings at four hour intervals and limits the daily quantity to one liter of mixture. After 6 months he also allows broths, fruits and vegetables. Porter²⁷ also considers 32 ounces of milk the greatest daily ration any baby should have, with 8 ounces as the maximum feeding. He begins cereals and fruits at about 10 months. He starts on seven feedings a day and reduces rapidly to six or five. Grulee³⁵ never gives over a quart of milk in twenty-four hours and rarely over 1½ pints; that is 1½ ounces of whole milk to the pound of body weight, with ¾ to 1¼ ounces of carbohydrate, for the normal baby. The rest of the food should be cereals and vegetables. Darling³¹ considers cow's milk unmodified or modified by dilution or removal of part of its fat content, a suitable infant food. Hanbidge³⁶ has had thirty-five infants do well on undiluted cow's milk, while only four did not do well on it. He believes that the lack of dilution greatly helps digestion. Shaw³⁷ states that some babies thrive on mixtures which in others would produce serious if not fatal results. The success of any system of feeding depends on the manner in which it is applied rather than on the method itself. Wieland⁷ also believes that the proper administration of the food (at regular intervals and in correct amount) is as important as is the choice of the special mixture. Johnston³⁸ advises judging the correctness of the feeding by the weight, the temperature and the stools. Courtney³⁹ says one should be guided by general rules of infant feeding, paying only secondary attention to the appearance or disappearance of curds in the stools. Abt³² believes, in order to feed an infant successfully, one must have a definite knowledge of his digestive functions and his constitutional state. Knowledge of the physiology of food, the injuries produced by food and the tolerance for food is also requisite. Overfeeding, which Porter²⁷ considers more common than underfeeding, is as disastrous as underfeeding. Every baby should be studied as an individual. He may be difficult to feed because he is suffering from an inherited disease, an anatomic malformation, a constitutional vice or an infectious disease. Fresh air, intelligent care, good housing, frequent bathing, cleanliness and proper clothing are powerful adjuvants in all that pertains to normal digestion and the upbuilding processes of infants. Spriggs⁴⁰ also lays stress on correct hygiene in the feeding in difficult cases. Benson⁴¹ fed 400 infants in the Babies' Dairies of New York City on seven ascending

35. Grulee, C. G.: *Journal-Lancet*, 1912, xxxii, 141.

36. Hanbidge, W. B.: *New York State Jour. Med.*, 1912, xii, 188.

37. Shaw, H. L. K.: *Albany Med. Ann.*, 1912, xxxiii, 13.

38. Johnston, C. H.: *Physician and Surg.*, 1911, xxxiii, 353.

39. Courtney, A. M.: *AM. JOUR. DIS. CHILD.*, 1912, iii, 1.

40. Spriggs, A. I.: *Clin. Jour.*, 1911, xxxix, 57.

41. Benson, R. A.: *Am. Jour. Obst.*, 1911, lxiv, 1084.

dilutions of the upper 16 ounces from a quart (7 per cent. fat); then on three dilutions of whole milk. Many babies can digest whole milk at 3 or 4 months of age and most infants at 6 months. He used no lime water; water as diluent for the first month, then barley water. The milk stations of the Boston Milk and Baby Hygiene Association¹⁶ supply whole milk and various formulas. They hold weekly conferences on keeping babies well, and give talks on prophylaxis and hygiene, educational work which is giving excellent results. Davis¹⁵ noted that bottle-fed babies from one to three months of age gave the highest mortality.

Fat.—While most physicians still keep the fat percentage cautiously low, Ladd⁴² has had excellent results, even in atrophic infants, on higher percentages of fat than are ordinarily given. Stolte⁴³ believes that infants will thrive on any food which causes soap production in the feces, with the absence of fermentation. The essential point is the proper balance between the fat and lime salts in the intestines to bring about saponification.

Sugar.—Benson⁴¹ reports good results on milk-sugar in his 400 cases. Ladd⁴² found that, in atrophic infants, the average rate of gain on whey mixtures with lactose was 26 per cent. less than on similar whey mixtures with maltose. Schlutz,⁴⁴ after prolonged studies, concludes that lactose possesses no distinct pyrogenic action. Leopold⁴⁵ reports seven infants in whom excellent results were obtained on milk mixtures containing dextrimaltose. Neff⁴⁶ thinks that maltose will answer all requirements for infant feeding.

Mixed Carbohydrates.—Keller's malt-soup and other mixtures containing flour, oatmeal water and dextrimaltose are considered excellent by Levy,³⁴ Grulee,³⁵ Neff^{46, 47} and Brady.⁴⁸ Brady has used Keller's malt-soup with success even in marasmus. After two or three months he changes to a milk mixture with high sugar. Grulee³⁵ describes the preparation of wheat flour and considers that fermentation is less active when this is used in place of barley flour. The various carbohydrates are absorbed one after the other. This may prevent a sudden taxing of the organism by a rapid absorption of one digestion product. Stolte⁴³ says "the more complex the carbohydrate, the longer is fermentation postponed." This explains the great value of mixtures of dextrimaltose and flour.

42. Ladd, Maynard: Arch. Pediat., 1912, xxix, 324.

43. Stolte, K.: Jahrb. f. Kinderh., 1911, lxxiv, 367.

44. Schlutz, F. W.: AM. JOUR. DIS. CHILD., 1912, iii, 95.

45. Leopold, J. S.: Arch. Pediat., 1911, xxviii, 844.

46. Neff, F. C.: Medical Herald, 1912, xxxi, 24.

47. Neff, F. C.: Jour. Am. Med. Assn., 1911, lvii, 2068.

48. Brady, J. M.: Jour. Am. Med. Assn., 1912, lviii, 751.

Proteid.—Hunt¹ details the methods employed to aid protein digestion; boiling the milk, adding cereals, adding alkalies in small quantity, partially peptonizing, using whey, buttermilk or equal parts of human and cow's milk. Each child must be considered as an individual and the method adopted must be the one best fitted to the needs of the particular infant. Porter²⁷ gives 1¼ ounces of protein-containing fluid per pound per day. Boggs⁴⁹ advises split protein for babies under 7 months; then he changes to top milk mixtures. Ruhräh⁵⁰ reports success from soy bean in the form of a dilute gruel, with or without milk added. It may be of use when milk disagrees. Each ounce of soy bean flour yields about 13 gm. of protein and 120 calories.

Albumin Milk.—The Germans report excellent results on Finkelstein's albumin milk. Benfey⁵¹ gave it to forty-four normal infants from birth, all doing well, and to thirty-nine new-born infants with infections, 71 per cent. of whom did well. He gives 150 to 200 gm. for each kilogram of body weight daily, with malt-sugar up to 6, 7 or 8 per cent. Beck⁵² gave it to 175 infants, with only twelve deaths. The quantity of food and the sugar in it should be rapidly increased. Haimis⁵³ found it of value in chronic nutritional disturbances. Schlutz⁵⁴ has seen only good results on it in diarrhea; Heiman⁵⁵ observed some improvement on it, while Neff⁴⁷ considers that it has a limited field in cases of catarrhal enteritis. Morse⁵⁶ reports eight infants fed on a laboratory milk with high casein and malt-sugar. He considers that withdrawing the lactose and increasing the percentage of casein, followed by adding dextrimaltose, is a valuable method of treating intestinal disturbances associated with fermentation in infancy. As babies will not thrive on such mixtures, they should be discontinued as soon as symptoms are relieved. He believes that this method is not generally applicable. Heim and John⁵⁷ fed a milk made by adding the fat and casein from ⅔ liter of raw milk mixed with ⅔ liter of water, to ⅓ liter of boiled milk, to five infants, all of whom gained in weight and did well.

Lactalbumin.—Sill⁵⁸ added powdered lactalbumin to milk mixtures for infants who were ill-nourished and markedly under weight, all of them gaining well on it. Bornstein⁵⁹ performed numerous metabolism

49. Boggs, W. D.: Calif. State Jour. Med., 1911, ix, 496.

50. Ruhräh, John: Arch. Pediat., 1911, xxviii, 841.

51. Benfey, Arnold: Jahrb. f. Kinderh., 1912, lxxv, 280.

52. Beck, Carl: Jahrb. f. Kinderh., 1912, lxxv, 315.

53. Haimis, G.: Gyógyászat, 1911, No. 15.

54. Schlutz, F. W.: Journal-Lancet, 1912, xxxii, 181.

55. Heiman, H.: Arch. Pediat., 1911, xxviii, 964.

56. Morse, J. L.: AM. JOUR. DIS. CHILD., 1911, ii, 315.

57. Heim, P., and John, K. M.: Ztschr. f. Kinderh., 1912, iv, 1.

58. Sill, E. M.: New York Med. Jour., 1912, xcv, 1093.

59. Bornstein, K.: Arch. f. Kinderh., 1911, lvi, 16.

experiments on three infants using a proprietary form of lactalbumin. He concludes that it causes more frequent and less consistent stools, but that, in spite of the increased quantity of protein ingested, the excretion of feces, as well as of calcium and nitrogen, is not changed.

Boiled Milk.—Ladd⁴² notes that babies on boiled milk did as well as those on the same mixtures unboiled. Abt⁴³ thinks that scalded or boiled milk sometimes agrees when raw cow's milk causes indigestion and diarrhea. Hunt¹ finds that artificial gastric digestion experiments show that boiling the milk decreases the amount of soluble calcium salts and removes any carbon dioxid present. Rudolf,⁶⁰ who advocates low percentages in infant feeding, favors using boiled milk and quotes many English authorities who have used undiluted sterilized cow's milk successfully. Verley⁶¹ reports a ten-day-old infant who, failing to gain on milk and barley-water, did well on whole milk, sterilized. Benson,⁴¹ in his series of 400 babies, neither pasteurized nor sterilized any of his formulas. Schorer and Rosenau⁶² believe that all commercial pasteurizing plants should be under official control and standardized. The best temperature to meet practical conditions is 145 F. for thirty to forty-five minutes. While Schorer⁶³ considers it safest to pasteurize in the sealed bottle, Schulz⁶⁴ found that as much as 0.03 gm. of silicic oxid passed into the milk when it was sterilized in the sealed bottle. He thinks this may help to explain the obstinate constipation and possibly infantile scurvy which may occur. Jordan⁶⁵ notes an instance of infantile scurvy occurring in a baby fed only on sterilized milk.

Desiccated Milk.—Nageotte-Wilbouchevitch⁶⁶ and Aviragnet, Bloch-Michel and Dorlencourt⁶⁷ have had success with dried milk in powdered and tablet form. The former used it for children who could not take milk without symptoms of intoxication. The latter have employed it for three years in both well and ill infants. It was most successful in cases of enteritis with vomiting. The powder contains less than 4 per cent. water. There are three varieties of desiccated milk, made from whole and skimmed milk. But prolonged feeding of such dried, sterile food is exceedingly dangerous.

Buttermilk.—Neff⁶⁸ advises buttermilk in marasmus, chronic colitis, the "exudative diathesis" and difficult feeding cases. It is, however, not

60. Rudolf, R. D.: Canadian Med. Assn. Jour., 1912, ii, 173.

61. Verley, R. G.: British Med. Jour., 1912, i, 831.

62. Schorer, E. H., and Rosenau, M. J.: Jour. Med. Research, 1912, xxvi, 127.

63. Schorer, E. H.: AM. JOUR. DIS. CHILD., 1912, iii, 226.

64. Schulz, H.: München. med. Wchnschr., 1912, lix, 366.

65. Jordan, W. R.: Brit. Jour. Child. Dis., 1911, viii, 520.

66. Nageotte-Wilbouchevitch: Bull. Soc. de pédiat. de Paris, 1912, xiv, 23.

67. Aviragnet, E. C., Bloch-Michael, L., and Dorlencourt, H.: Bull. Soc. de pédiat. de Paris, 1912, xiv, 109.

68. Neff, F. C.: Jour. Missouri State Med. Assn., 1911, viii, 160.

a substitute for sweet milk. It is well tolerated in hot weather. Clean, fresh milk must be used for preparing the buttermilk and top milk may be added gradually, if desired. When breast milk is not available, Neff⁶⁷ uses buttermilk in cases of fat intolerance and enterocolitis. Heinemann⁶⁹ states that many of the ferments sold for making sour milk are worthless. The fermented milks are only of value in infancy because of their low fat content.

Vacuum Bottles.—Tonney and Pillinger⁷⁰ advocate the use of the vacuum bottle in infant feeding, if controlled by a thermometer. It not only keeps the milk warm, but effectually pasteurizes it. It will maintain a proper temperature (about 115 F.) for ten hours. If the milk, on testing with the thermometer, is found under 115 F., it should not be used.

Card for Calculating Mixtures.—Young⁷¹ has devised a card which reduces mathematics to a minimum. The celluloid envelope contains two celluloid cards, printed on each side, for making 20, 32, 40 and 48 ounce mixtures, with milk and cream, or with whey. Any formula can rapidly be worked out with this card, together with the total caloric value of the mixture. The card is to be commended because no attempt is made to suggest any formula for a baby of any age or weight.

Caloric Values.—Fraley's⁷² formula for calculating the total caloric value of percentage mixtures is exceedingly simple. He adds together twice the fat, the sugar and the protein; and then multiplies by $1\frac{1}{4}$ times the total quantity ingested in twenty-four hours, with a result which is the total caloric value of the day's feedings. $(2F+S+P) \times 1\frac{1}{4}Q = C$. Farr⁷³ has collected all the foods used in childhood and demonstrates their comparative caloric values exceedingly well, both by photographs and tables. English⁷⁴ has prepared detailed diet lists for children from 2 to 15 years of age, advising regular meals, sufficient mastication, little fluid at meals and nothing between meals except water. Stargardt⁷⁵ has made several feeding and metabolism experiments to show the amount of food and of protein required by children. He gives tables showing the number of calories necessary and diets for children of two and seven years. Hoobler⁷⁶ gives a list of foodstuffs containing phosphorus, potassium, sodium, iron, sulphur, chlorine, magnesium and calcium, noting the percentage of the mineral salt in each kind of food. He suggests using these foodstuffs therapeutically in diseases in which there is a

69. Heinemann, P. G.: Jour. Am. Med. Assn., 1912, lviii, 1252.

70. Tonney, F. O., and Pillinger, H. H.: Jour. Am. Med. Assn., 1912, lviii, 1495.

71. Young, J. H.: Boston Med. and Surg. Jour., 1912, clxvi, 372.

72. Fraley, F.: Arch. Pediat., 1912, xxix, 123.

73. Farr, Clifford B.: Arch. Pediat., 1912, xxix, 110.

74. English, D. E.: Jour. of the Med. Soc. of New Jersey, 1911, viii, 354.

75. Stargardt, Julius: Arch. f. Kinderh., 1912, lvii, 305.

76. Hoobler, B. R.: Arch. Pediat., 1912, xxix, 208.

known deficiency in mineral salts. Those containing salts of iron will be employed with least difficulty, since they are of use in secondary anemia.

DISORDERS OF THE DIGESTIVE SYSTEM

Stomatitis.—Kerr⁷⁷ divides stomatitis into acute catarrhal stomatitis, stomatitis mucosa, stomatitis unaccompanied by odor or ulceration, stomatitis with ulceration and no offensive odor, syphilitic stomatitis, stomatitis ulcerosa, stomatitis gangrenosa and stomatitis with membrane formation. Gaujoux⁷⁸ differentiates between simple aphthous stomatitis and "foot and mouth disease." In the former, due to some error in diet, the treatment is a mild antiseptic wash. In the latter, which is generally traceable to an infected milk-supply, all milk should be boiled, and sodium salicylate and occasionally diphtheria antitoxin should be administered.

Foreign Bodies in Esophagus.—Abrand⁷⁹ reports the cases of two children who swallowed pieces of bone about an inch long, which lodged in the esophagus. The first case was a boy of 12 years, who vomited the bone two days later. In the second case the bone was readily removed under anesthesia.

Pyloric Stenosis.—Leavitt and Porter⁸⁰ studied twenty-four infants with muscular pyloric hypertrophy. They conclude that those babies who retain the regurgitant type of vomiting do better than those in whom the vomiting is constantly cumulative and propulsive. They were impressed with the need of a uniform method of studying and reporting cases of congenital pyloric spasm and hypertrophy. Lapage⁸¹ outlines the medical treatment as careful regulation of feeding, with easily digested food, in small quantities at first; lavage; saline infusion by rectum or subcutaneously; brandy; cod-liver oil inunctions and perhaps opium or belladonna. Bilderback⁸² reviews the subject. Operative cases are reported by Gavin,⁸³ a baby of 7 weeks recovering after posterior gastrojejunostomy; Bunts,⁸⁴ seven cases, with four recoveries; Cotiguola,⁸⁵ three cases with one recovery; Katzmman and Abell,⁸⁶ an infant of 6 weeks who died thirty-one hours after pyloroplasty; Smedley,⁸⁷ an infant of 6 weeks, with death from enterocolitis two weeks after posterior gastro-

77. Kerr, Legrand: Am. Med., 1912, xviii, 108.

78. Gaujoux, E.: Ann. de méd. et de chir. infant., 1912, xvi, 1.

79. Abrand, H.: Bull. Soc. de pédiat. de Paris, 1912, xiv, 16.

80. Leavitt, W. B., and Porter, L.: Jour. Am. Med. Assn., 1912, lviii, 256.

81. Lapage, C. P.: Practitioner, London, 1912, lxxxviii, 401.

82. Bilderback, J. B.: Medical Sentinel, 1911, xix, 744.

83. Gavin, G. E.: Southern Med. Jour., 1912, v, 241.

84. Bunts, F. E.: Am. Jour. Med. Sc., 1912, cxliii, 14.

85. Cotiguola, M. F.: Semana méd., 1912, xix, 489.

86. Katzmman, E. F., and Abell, T.: Kentucky Med. Jour., 1911, ix, 804.

87. Smedley, R. C.: Northwest Med., 1912, iv, 5.

enterostomy. Tanaka⁸⁸ reports two more fatal cases. Hoffa⁸⁹ reports five interesting cases of visible gastric peristalsis, without vomiting or pyloric stenosis. He concludes that visible gastric peristalsis does accompany pylorospasm and does not necessarily denote pyloric stenosis. Graham⁹⁰ reports a case of persistent vomiting in a boy of 6½ years in whom no lesion of the pylorus or stomach was found post mortem. Sarcoma of one eye had been operated on two months before vomiting began and sarcoma of the liver was found at autopsy. Graham believes that pyloric stenosis occurs in children and young adults more commonly than is supposed; that it may remain latent for years; that the entire disappearance of all symptoms and the apparent health of the infant during childhood suggest the probability of absorption of the hypertrophy.

Habitual Vomiting.—Lowenburg⁹¹ considers irregular feeding and overfeeding responsible for the vast majority of cases of functional vomiting in infants under 1 year of age. In older children some indiscretion in diet is the common cause of vomiting. Cheinisse⁹² considers habitual vomiting in infants generally due to overfeeding; but it may be due to insufficient nourishment or to nervous hyperexcitability of the gastric mucosa, with or without pyloric stenosis. Hahn⁹³ found that less dilute food, such as milk, barley-jelly and sugar, containing 1,000 calories to the liter, was well borne by those infants in whom no organic cause for the vomiting could be found. Kevacs⁹⁴ also advises more consistent foods (milk or strained vegetables) rather than a diluted milk mixture. Smith⁹⁵ describes seven cases of nervous vomiting, occurring in neurotic children with enuresis, migraine, habit-spasm or rheumatism. The nervous inheritance is always present, associated with some other functional condition. Recovery follows good hygiene, elimination of the cause aggravating the underlying nervous instability and firm moral control.

Recurrent Vomiting.—Sedgwick,⁹⁶ as a result of his investigations, found that the creatin metabolism, the endogenous nitrogen metabolism, is abnormal during attacks of recurrent vomiting. In many cases the removal of adenoids has been followed by cessation of the attacks of recurrent vomiting. Morris⁹⁷ calls attention to "prune juice" vomiting as a symptom of the cases of recurrent vomiting which he has observed.

88. Tanaka, Tamio: *Jahrb. f. Kinderh.*, 1912, lxxv, 18.

89. Hoffa, T.: *Monatschr. f. Kinderh.*, 1912, x, 523.

90. Graham, E. E.: *AM. JOUR. DIS. CHILD.*, 1911, ii, 407.

91. Lowenburg, H.: *Jour. Am. Med. Assn.*, 1912, lviii, 180.

92. Cheinisse, L.: *Semaine méd.*, 1911, xxxi, 565.

93. Hahn, H.: *Med. Klin.*, 1911, No. 38.

94. Kevacs, B.: *Gyógyászat*, 1911, No. 43.

95. Smith, Eric B.: *Lancet*, London, 1911, ii, 1769.

96. Sedgwick, J. P.: *AM. JOUR. DIS. CHILD.*, 1912, iii, 209.

97. Morris, R. S.: *Am. Jour. Obst.*, lxxv, 534.

Nesbitt⁹⁸ reports the case of a baby thirty hours old who vomited bright red blood; then passed dark masses in the stools up to 3 days of age; who grew up well afterward. Hess⁹⁹ advises the duodenal catheter (a soft rubber Nélaton catheter, No. 15) in the differential diagnosis between cases of vomiting due to pylorospasm and those cases not due to spasm of the pylorus. Cardiospasm often accompanies pylorospasm. Duodenal feeding is of value in cases of persistent vomiting with marked inanition. Lust¹⁰⁰ reports a case of "rumination" in an infant of 5½ months, with increasing malnutrition and death at 8 months.

Liver: Jaundice.—Hess¹⁰¹ observed 124 infants with icterus neonatorum. By using the duodenal catheter he found that bile was excreted during the first twelve hours of life. During the next twenty-four hours the amount excreted is profuse if icterus is present; scanty or absent when there is no jaundice. The function of bile excretion becomes fully established during the first week or ten days. The appearance of jaundice precedes the excretion of bile into the duodenum. Raynaud and Coudray¹⁰² report a case of catarrhal jaundice in a girl of 4 years, with a typical tetragenus found in blood cultures, which was agglutinated by the patient's blood-serum. Talbot¹⁰³ reports a case of acute intestinal indigestion in a boy of 10 years, ill six weeks, eating ten or more apples daily. For two weeks fever and headache had been noted, while jaundice appeared one week previously. On excluding fat and sugar from his diet, he gained 5 pounds in twelve days, his food being restricted to meat, starches and skimmed milk. Urobilinogen was absent from the urine while there was complete obstruction to bile, which then appeared in excessive amounts when the obstruction was removed.

Cirrhosis.—Lahiri¹⁰⁴ reports a case of cirrhosis of the liver in an infant 18 months old, ill eight months. There was marked ascites. On three injections into the cellular tissue of the flank of the child's own serum, first ½ c.c.; eight days later 1 c.c., and five weeks later 2 c.c.; complete recovery followed. Pagliano and de Luna¹⁰⁵ report the case of a boy of 12 years, with hepatic cirrhosis, without any history of syphilis, malaria or alcohol. The condition had persisted for years, without the boy having grown up. Sukares¹⁰⁶ reports the autopsy on a child of 2 years in whom the diagnosis of tuberculosis had been made. The only lesion found was hepatic cirrhosis of the rare microsplenic, anicteric type.

98. Nesbitt, M. D.: Australasian Med. Gaz., 1911, xxx, 514.

99. Hess, A. F.: AM. JOUR. DIS. CHILD., 1912, iii, 133.

100. Lust, F.: Monatschr. f. Kinderh., 1911, x, 316.

101. Hess, A. F.: AM. JOUR. DIS. CHILD., 1912, iii, 304.

102. Raynaud, M., and Coudray, M.: Progrès méd., 1911, 206.

103. Talbot, F. B.: AM. JOUR. DIS. CHILD., 1912, iii, 398.

104. Lahiri, M.: Practitioner, London, 1912, lxxxviii, 478.

105. Pagliano and de Luna: Ann. de méd. et chir. Inf., 1912, xvi, 212.

106. Sukares, O.: Gyógyászat, 1911, No. 44.

Acute Yellow Atrophy.—Two fatal cases are reported, one by Phillips¹⁰⁷ in a girl of 5 years, who died in one week; the other by Drennan¹⁰⁸ in a boy of 8 years, with death in one month.

Appendix.—McPherson¹⁰⁹ describes an appendix found at the autopsy of a 15-hour-old baby. It was adherent by many fibrous bands to the posterior aspect of the cecum and assumed a horse-shoe shape. Kee¹¹⁰ has removed the appendix from twenty-three children between 2½ and 13 years of age. In twenty cases the appendix was perforated, gangrenous or ulcerated, with abscess; six of these died. Canaguier and Hamel¹¹¹ report the removal of the appendix from an infant five days old, with death a week later. Rheindorf¹¹² found oxyuris in the appendix in six out of thirteen bodies of children between 3 and 12 years of age who died from acute appendicitis. He thinks more efforts should be made to keep the intestines of children free from seat-worms.

Intussusception, Etc.—Kakels¹¹³ reports operating on the third day on a girl of 5 years with intussusception, who was well in three weeks. He resected 12 inches of gangrenous intestine, the ileum having passed through the ileocecal valve. An adenoma was found in the intestine at the apex of the intussusception. King¹¹⁴ reduced an intussusception in a boy of 11 weeks by operating eight hours after the onset of the attack, also removing a strangulated appendix. Recovery was uneventful. Dunn¹¹⁵ reports operating after six days of illness on a boy of two years, resecting 6 inches of small intestine, with death in forty-eight hours. A Meckel's diverticulum, 2 inches long, had invaginated into the small intestine. Guinon and Fauquez¹¹⁶ report late operation, with death, on an infant of 5½ months with acute invagination. Weill-Hallé¹¹⁷ reports another fatal case in an infant of 11 months, ill only twenty-four hours; Grisel¹¹⁸ one case in an infant of 7 months who died two days after operation and another, a boy of 12 years, who recovered without operation. O'Neill¹¹⁹ reports the history of a colored boy of 15 months, in whom what was supposed to be intussusception proved to be a small china pig the child had swallowed. This was passed successfully, complete recovery

107. Phillips, John: *Am. Jour. Med. Sc.*, 1912, cxliii, 177.

108. Drennan, A. M.: *Jour. Path. and Bacteriol.*, 1911, xvi, 141.

109. McPherson, Ross: *Bull. of the Lying-In Hosp., City of New York*, 1912, viii, 67.

110. Kee, A. L.: *West. Med. Rev.*, 1912, xvii, 125.

111. Canaguier and Hamel: *Bull. Soc. de pédiat.*, Paris, 1912, xiv, 45.

112. Rheindorf: *Berl. klin. Wehnschr.*, 1912, xlix, 450 and 503.

113. Kakels, M. S.: *Am. Jour. Surg.*, 1911, xxv, 363.

114. King, J. C.: *Southern Cal. Practitioner*, 1912, xxvii, 57.

115. Dunn, L. A.: *Clin. Jour.*, 1912, xxxix, 350.

116. Guinon and Fauquez, *Bull. Soc. de pédiat. de Paris*, 1911, xiii, 361.

117. Weill-Hallé: *Bull. Soc. de pédiat. de Paris*, 1911, xiii, 369.

118. Grisel, P.: *Bull. Soc. de pédiat. de Paris*, 1911, xiii, 436.

119. O'Neil, Owen: *Yale Med. Jour.*, 1911, xviii, 254.

resulting. He also reports two cases of intussusception with operation, in a girl of 4 months who died of enterocolitis fourteen days later, and a boy of 8 months who recovered. Comby¹²⁰ reports a case of chronic invagination in a girl of 4 years, in whom the condition was supposed to be ileocolitis. She was ill twenty-six days, suffering from pain, vomiting and diarrhea, with blood and mucus in the stools. Triboulet and Savariaud¹²¹ describe another case of chronic invagination in a boy of 5½ years, easily reduced at operation. Matheny¹²² reports eight cases of intussusception with only two deaths after operation. Early diagnosis and operation are essential to a low mortality. As the mesentery in childhood is long, violent pitching or swinging of children should be avoided. He also lays stress on digital examination per rectum whenever a child has abdominal pain. Other causes of abdominal pain in children are given by Finkelstein¹²³ as appendicitis, disease of the large or small intestine, neuralgia of the spinal nerves due to caries, dyspepsia, intestinal stenosis following circumscribed tubercular peritonitis, and renal colic. Kirmisson¹²⁴ describes excising a persistent Meckel's diverticulum which opened at the umbilicus, in an infant of 1 month, with recovery. Waugh¹²⁵ reports a rare case of congenital hernia of the cord, causing acute intestinal obstruction. Spinal anesthesia was used and enterectomy (lateral anastomosis) done. While the baby recovered from the operation, it died a month later of marasmus. Wilcox¹²⁶ operated on an infant 48 hours old, who vomited continually. The entire large intestine was found to be only a fibromuscular cord. Death followed two hours after operation. Hauser¹²⁷ found total atresia of the duodenum at autopsy in a baby 7 days old who had vomited persistently since birth. Kermanner¹²⁸ also describes a case of congenital atresia of the duodenum. A case of fatal duodenal ulcer in an infant of one month, who died of intestinal hemorrhage, is described by Weill and Gardère.¹²⁹ Sheffield¹³⁰ describes a monstrosity in which no anus could be found. Law¹³¹ reports two cases of imperforate anus in girls of 3½ and 13 years, the intestine opening into the vagina. While the larger one recovered after operation, the

120. Comby, Jules: *Arch de méd. des enf.*, 1912, xv, 47.

121. Triboulet and Savariaud: *Bull. Soc. de pédiat. de Paris*, 1912, xiv, 136.

122. Matheny, A. R.: *Pennsylvania Med. Jour.*, 1912, xv, 440.

123. Finkelstein, F.: *Zentralbl. f. Kinderh.*, 1912, xvii, 1.

124. Kirmisson, E.: *Bull. de l'académie Méd.*, 1912, lxxviii, 143.

125. Waugh, George E.: *Lancet*, London, 1912, I, 427.

126. Wilcox, G. A.: *Jour. Med. Assn. of Georgia*, 1911, i, 145.

127. Hauser, Hans: *Monatschr. f. Geburtsh. und Gynäk.*, 1911, xxxiv, 678.

128. Kermanner, F.: *Virchows Arch. f. path. Anat.*, 1912, ccvii, March.

129. Weill and Gardère: *Ann. de méd. et chir. inf.*, April 15, 1912, xvi.

130. Sheffield, H. B.: *Med. Rec.*, New York, 1911, lxxx, 1164.

131. Law, A. A.: *Journal-Lancet*, 1912, xxxii, 202.

smaller died in thirty-five days from septic nephritis. Farnsworth¹³² reports two similar cases, in girls of 3 weeks and 3 years.

Megacolon.—Three cases are described in recent German literature, all successfully treated. Göppert's¹³³ case was a boy of 3½ years with constipation and enormous distention of the colon, due to a bend in the descending colon which prevented defecation. The daily passage of a rectal tube during several months was followed by regular normal defecation since. Hoffmann¹³⁴ describes two cases in which resection of the sigmoid and upper rectum was performed, with recovery. In one, a boy of 14, 30 cm. of intestine was resected. Sheffield¹³⁵ also operated on his patient, with death the next day. He found the descending colon widely dilated, cornet shaped, with its wide extremity (6½ inches in circumference) terminating at the sigmoid.

Enteroptosis.—Smith¹³⁶ studied 109 girls under 13 years of age and found that children with a tendency to enteroptosis show frailness, lack of fat, slenderness of muscle and lack of vigor in body development. He recommends special attention to frail children very early, with continual treatment to make them more robust. Marfan¹³⁶ describes a condition which he calls the "large flaccid abdomen of infants," found in babies with rickets, but to be distinguished from the large tympanitic abdomen of infancy. It is an atonic condition of the abdominal muscles and is due to recurrent attacks of catarrhal gastro-enteritis. At autopsy the intestine is found to be from ⅓ to ½ as long as is normal, from atony of the intestinal musculature, analogous to the gastric dilatation also present in most of these infants.

Constipation.—Périer and Gaujoux¹³⁷ consider constipation due to obstruction, to modification of the contents of the intestine and to defective action of the muscles or nerves of the intestines. They found that congenital stenosis of the rectum may escape discovery for weeks or even months. Ward¹³⁸ reports twelve children with joint tuberculosis, one with rheumatoid arthritis and one with ulcerative colitis, all with marked intestinal stasis. He performed ileocolostomy on all with recovery.

Diarrhea.—Forsyth¹³⁹ considers infantile diarrhea due to an infection following overfeeding or irregular feeding. Bilderback¹⁴⁰ states that impure milk causes diarrhea; heat and overfeeding or improper feeding

132. Farnsworth, C. P.: Med. Rec., New York, 1912, lxxxi, 470.

133. Göppert, F.: Berl. klin. Wchnschr., 1912, xl, 588.

134. Hoffmann, H.: Beitr. z. klin. Chir., 1911, lxxvi, 533.

135. Smith, R. R.: Jour. Am. Med. Assn., 1912, lviii, 385.

136. Marfan, A. B.: Arch. de méd. des enf., 1911, No. 8.

137. Périer, E., and Gaujoux: Ann. de méd. et chir. inf., 1911, xv, 593.

138. Ward, E. B.: Practitioner, London, 1912, lxxxviii, 570.

139. Forsyth, R. L.: Australian Med. Jour., 1912, ii, 289.

140. Bilderback, J. B.: Northwest Med., 1911, iii, 310.

aggravate it. Salle¹⁴¹ has performed experiments on animals to show the direct injury done to the gastric function by heat. As even slight changes in the food may be dangerous when the function of the digestive apparatus is disturbed by hot weather, less food should be given and more water is necessary. Wood¹⁴² considers the cause of summer diarrhea to be the high bacterial content of the milk. Grulee³⁵ considers milk-sugar responsible for many cases of summer diarrhea.

Rolleston and Molony¹⁴³ describe eleven cases of fatal purpura complicating infectious diarrhea. Symptomatic purpura occurs mainly on the abdomen and chest in infants under 1 year of age. It is usually a terminal phenomenon in prolonged cases. The prognosis is extremely grave.

Synnott¹⁴⁴ lays stress on pasteurizing or sterilizing even a clean milk in hot weather. Dennett¹⁴⁵ advises a milk and water mixture, boiled, without any sugar, for poorly nourished infants. The well nourished babies do best on barley gruel for a few days. Stephens¹⁴⁶ gives water only, then cereals or albumins and finally milk. Synnott¹⁴⁴ advises water in abundance, intestinal irrigation in many cases, isolation of the baby and disinfection of all sick-room implements. Machell¹⁴⁷ makes a plea for the short rectal tube, since a larger amount can be injected and it is retained longer when a short nozzle is used. Albumin milk is advised by Stolte,⁴⁸ Neff,⁴⁷ Beck,⁵² Schlutz,⁵⁴ Heiman⁵⁵ and Dennett.¹⁴⁵ Buttermilk is also advised by Neff⁴⁷ and Stolte.⁴⁸ Brady⁴⁸ recommends malt-soup in diarrhea. Ruhräh⁵⁰ recommends soy bean flour. Nageotte-Wilbouchewitch⁵⁶ and Aviragnet, Bloch-Michel and Dorlencourt⁵⁷ had good results with desiccated milk in powder and tablet form.

Synnott¹⁴⁴ gives castor oil and advises antidysenteric serum in certain cases. Dennett¹⁴⁵ believes that cathartics should always be given to babies with diarrhea with great discretion. He recommends them in the infectious diarrheas, with starvation for forty-eight hours only. Wood¹⁴² uses no drugs except opium when necessary. Hand¹⁴⁸ speaks of the value of bismuth salicylate as an intestinal antiseptic in acute diarrhea. Thymol and salol are too irritating and calomel is not advised. Grulee and Buhlig¹⁴⁹ conclude from their observations on milk that sodium benzoate (1 grain to 6 ounces of milk) must have a slight effect in inhibiting some kinds of bacteria, because of the difference in the time the milks

141. Salle, V.: *Jahrb. f. Kinderh.*, 1911, lxxiv, 697.

142. Wood, A. J.: *Australian Med. Jour.*, 1912, ii, 263 and 278.

143. Rolleston, H. D., and Molony, J. B.: *Brit. Jour. Child. Dis.*, 1912, ix, 1.

144. Synnott, M. J.: *Arch. Pediat.*, 1911, xxviii, 989.

145. Bennett, Roger H.: *Med. Rec.*, New York, 1911, lxxx, 1138.

146. Stephens, H. D.: *Australian Med. Jour.*, 1912, ii, 288.

147. Machell, H. T.: *Arch. Pediat.*, 1911, xxviii, 837.

148. Hand, Alfred Jr.: *Arch. Pediat.*, 1912, xxix, 148.

149. Grulee, C. G., and Buhlig, W. N.: *Arch. Pediat.*, 1911, xxviii, 849.

become sour and coagulated; that sodium benzoate seems to be a fair preservative only when very few living bacteria are present. From their clinical observations on nine infants from a few weeks to almost 2 years of age, they found that $2\frac{1}{2}$ to 5 grains of sodium benzoate in twenty-four hours produced no recognizable symptoms, even though the children were suffering from gastro-intestinal disturbances of a serious nature. Ellis¹⁵⁰ reports good results in the chronic forms of diarrhea on magnesium sulphate. Löbisch¹⁵¹ treated seven infants with summer diarrhea, aged 4 to 13 months, with hypertonic saline solution given intravenously to six and subcutaneously to one, with recovery. Rogers¹⁵² also recommends hypertonic saline injections, given intravenously, controlled by estimation of the specific gravity of the blood, in infantile diarrhea.

Infantile Atrophy.—Bar¹⁵³ considers athrepsia due to lack of production of ferments in the infant stomach. Cow's milk is an alien substance and acts as a poison unless ferments are present to modify it. The child becomes sensitized and the phenomena of anaphylaxis result. Sterilizing the milk will not prevent this action. Rarely, after prolonged illness during pregnancy, a mother's milk may also poison her baby. Czerny¹⁵⁴ considers atrophy not a disease *per se* but a disturbance in growth and general nutrition which is the result of nutritional disturbances or of infectious processes or of both. When the condition is a nutritional disturbance alone, splendid results may be obtained by dietetic management. The occurrence of atrophy is distinctly the result of a constitutional anomaly. Three classes of children suffer from it—those who inherit the "exudative diathesis," those of neuropathic or psychopathic parents and those with the "hydropic constitution." Atrophy is characterized by a cessation of normal growth throughout the entire organism, followed by a failure of the development of fat. Chapman¹⁵⁵ considers nutritional disturbances in infants either as disorders of alimentation, due to improper food, indigestion and failure of assimilation; or as disorders of infection, due to lack of cleanliness. Variot and Morancé¹⁵⁶ report twelve cases to show that the abdominal ectasia found in atrophic infants is due to hypo-alimentation. Both large and small intestines are distended. These infants need more food than heavier children and should be fed according to age and not to weight. Ladd¹⁵⁷ finds that the energy quotient is greatest when the weight development

150. Ellis, H. A.: Australasian Med. Gaz., 1912, **xxxi**, 30.

151. Löbisch, W.: Wien. klin. Wchnschr., 1911, **xxiv**, 1640.

152. Rogers, Leonard: Brit. Med. Jour., 1911, **ii**, 1404.

153. Bar, P.: Revue Mensuelle de Gynécologie, d'Obstetrique et de Pédiatrie, 1912, **vii**, 161.

154. Czerny, Ad.: AM. JOUR. DIS. CHILD., 1912, **iii**, 170.

is farthest from the average normal infant as determined by the weight chart. The quantity of food to be given an atrophic infant is only a little less than that which the normal infant of the same age receives and is often $1\frac{1}{2}$ to 2 ounces more than would be given the normal infant of the same weight.

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SOME FUNDAMENTAL PRINCIPLES IN STUDYING INFANT METABOLISM *

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Knowledge of the energy requirements of infants and the energy content of their food is of fundamental importance in studying their rate of growth and in the treatment of nutritional disorders.

The ideal method for determining the energy transformation of infants is that of direct measurement of the heat eliminated and produced. This involves expensive, elaborate apparatus, and has been possible in but one laboratory, that of Prof. Graham Lusk in New York. Undoubtedly, the cost of this extremely accurate and delicate apparatus will preclude its ever being used extensively in hospitals.

The other method that we wish to take up is that of so-called "indirect calorimetry," i. e., a computation of the energy transformations from the gaseous exchange. It is possible to compute with considerable accuracy the energy transformations of the infant from the amount of carbon dioxid produced, and particularly from the amount of oxygen consumed. Unfortunately, direct determinations of oxygen are difficult to carry out and require complicated apparatus. The direct measurement of oxygen in young infants has been but rarely determined. The principle work has been done by Professor Lusk¹ and an associate, Dr. John Howland,² in the respiration calorimeter at the Cornell University Medical School in New York, and recently in the respiration apparatus of Schlossmann and Murchauser³ in Düsseldorf.

Direct determinations of carbon dioxid produced by infants are less difficult and have frequently been made in a number of foreign laboratories. Nearly all of our knowledge of infant metabolism is based on these investigations.

*From the Nutrition Laboratory of the Carnegie Institution of Washington.

*Read at the meeting of the American Pediatric Society, Hot Springs, Va., May, 1912.

1. Howland: Proc. Soc. Exper. Biol. and Med., 1911, viii, 63.

2. Howland: Ztschr. f. physiol. Chem., 1911, lxxiv, 1.

3. Schlossmann and Murchauser: Biochem. Ztschr., 1908, xiv, 385; xviii, 1909, 489; 1910, xxvi, 14; 1911, xxxvii, 1 and 23; Schlossmann; Deutsch. Med. Wchnschr., 1911, p. 1633.

Practically all of the researches carried out on infants in which the carbon dioxide was measured, are open to serious objections, inasmuch as there was no proper control of the muscular activity.

In all previous determinations of infant metabolism, either of direct energy transformations or by means of the direct calorimetry, either no recognition has been given to the significance of muscular movements on

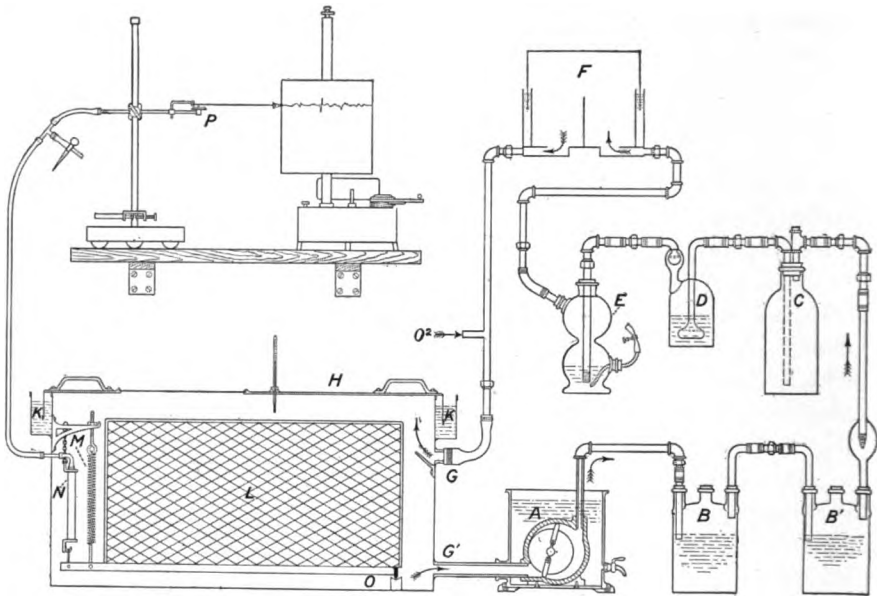


Fig. 1.—Diagram of respiration apparatus and absorbing system for determining the respiratory exchange of infants. The respiration chamber, L, in which the infant is placed is closed by a cover, H, which fits into a water seal, KK. One side of the cage, L, rests on a knife edge bearing, O, the other side being supported by a brass spring, M, fastened to a support. A tube pneumograph, N, is likewise attached to the cage, and any change in the center of gravity of the body of the infant produces an alteration in the tension of the spring, M, and the pneumograph, N. By air transmission, the tambour, P, moves a lever writing on the kymograph (the kymograph and tambour stand are drawn on a considerably enlarged scale). The air leaves the chamber at G', enters the rotary blower, A, and then passes through sulphuric acid in two Woulff bottles B and B'. It then passes through the carbon dioxide absorber, C, and next into the drying vessel, D. Moisture is added in the vessel, E. The air then passes through a spirometer, F, which allows for contraction or expansion of air in the system and then to the respiration chamber through the opening, G. Oxygen as required is supplied through the opening O.

the part of the child, or it has been assumed that the child when not crying or obviously restless, was quiet and with constant muscular activity. In other words, the notes accompanying these reports said that the baby was either crying or quiet, i. e., asleep. The difficulties incidental to securing long experimental periods of constant muscular activity with

infants are only too well known, and yet an examination of the literature shows that almost invariably all of the longer experiments on infant metabolism have included periods of obviously great muscular restlessness and activity, as well as periods of crying. While it is not necessary to show that the metabolism of an active crying infant must of necessity be considerably higher than that of a quiet child, it is not so well known that it is wholly illogical to compare the metabolism of an active, restless, normal baby with that of a quiet, sick baby, since the amount of carbon dioxid excreted depends on the degree of muscular activity.

It is our purpose in this paper to point out the inconsistencies arising from the determination of carbon dioxid in infants without taking muscular activity into consideration. We are disposed, therefore, to question the desirability of long experimental periods for establishing the basal metabolism of infants when such periods may include not only quiet sleep, but also periods of activity and even crying. It is necessary at the outset to find what is the ideal length of the experimental period in the infant. This, we consider, is the period in which the baby is asleep, absolutely quiet muscularly, and free from even the slightest tremor, and preferably without food in the stomach. And, although it is difficult to secure these ideal periods over any length of time, fortunately it can be demonstrated that if this condition exists for twenty minutes or more, a reasonably accurate measurement of the metabolism may be secured with modern perfected apparatus. The apparatus in which the experiments were made (Fig. 1) was a slight modification of that described by Benedict and Homans for experiments on hypophysectomized dogs.⁴

It was used primarily to determine the amount of carbon dioxid excreted in the air and was furnished with means of recording graphically the amount of motion of the infant. The baby was placed in a cradle or crib, *L*, one end of which was suspended on a knife edge, *O*, and the other by a stout spiral spring, *M*. Parallel to the spiral spring was a tube pneumograph, *N*, which was connected with a delicate tambour, *P*, on the outside. Any changes in position of the center of gravity of the infant produced alterations in the tension on the spring, and the pneumograph, which transmitted this change to the tambour and pointer which made a graphic record on a smoked paper drum. This pointer can be made very sensitive to motion by simple adjustment of the spring and the leverage of the tambour and, indeed, Benedict and Homans were able to obtain the respiration rate of their dogs from the record. This apparatus records the infant's slightest muscular tremors, and we were able to demonstrate that a baby could have considerable slight muscular motion, which was sufficient to affect the metabolism, and yet be imperceptible to the eye.

4. Benedict and Homans: Jour. Med. Research, 1912, xxv, 409.

The babies in these researches were normal (breast-fed) babies obtained from the directory for wet nurses of the Massachusetts Babies' Hospital. The mothers of these babies were the usual type of wet nurse, all of whom had had a complete physical examination and a negative Wassermann reaction in the blood. The babies were all breast-fed with the exception of one or two who had one bottle of modified cow's milk in the twenty-four hours.

A great many determinations of carbon dioxid were made, and although the babies were awake in the morning, they did not sleep for any length of time in the afternoon, and only one or two successful periods were obtained in this manner. It was eventually necessary to work at night in a semi-darkened room where the infants kept quieter and slept for a longer time than during the day. They were all fed just before being put in the respiration chamber and consequently the results are somewhat vitiated by the specific dynamic action of the food in the stomach. In no instance were they kept in the respiration chamber when they showed any signs of discomfort, and the mothers watched the babies during the entire time that they were under observation.

It has frequently been noted in this laboratory, both with animals and with men, that there is a definite relationship between the pulse-rate and metabolism; we therefore commenced to record the pulse-rates of the infants. These were taken with a Bowles stethoscope placed over the heart of the baby, the tube of which was carried through the wall of the respiratory chamber and connected with ear pieces outside. The beat was counted for a period of one minute every three or four minutes during the entire period of the experiment. The relationship between the pulse-rate and the metabolism of the infant was found to be very close. The question then came up as to what was the minimum pulse-rate of a given age and how much and how long it could be affected by muscular exercise. We could find no literature on this subject, and a series of investigations was, therefore, instituted by one of us (F. B. T.), in which the pulses of a number of babies were counted by a skilled nurse at the Boston Lying-In Hospital and at the Directory for Wet Nurses at the Massachusetts Babies' Hospital. The wide fluctuations found in the pulse-rate of the baby, even during periods of sleep, were astonishing, and a series of curves pointing out these pulse-rates are given herewith (Figs. 2 and 3).

The two curves given herewith are samples of a larger series and illustrate the effect of muscular exercise on the pulse taken with a Bowles stethoscope from the heart of a very young baby and that of an older baby. The most striking fact in comparing these two curves is that there is much less stability of the young babies' pulse than that of the older ones, and a slight motion causes more marked elevation of the pulse. The minimum average pulse-rate depends on the age and type of the baby,

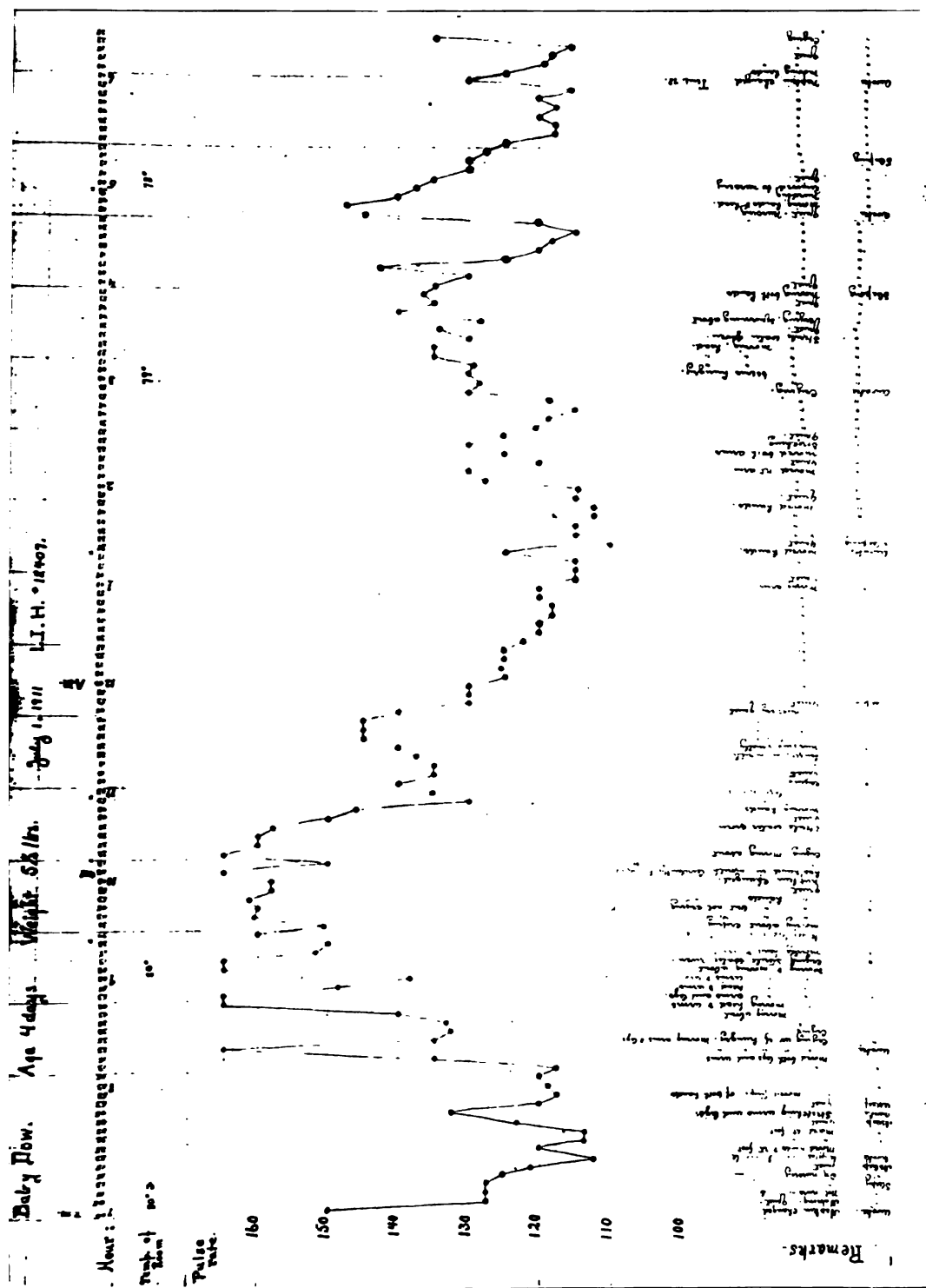


Fig. 2.—Pulse-chart of Infant Dow. Explained in the text.

and we believe that no general rules can be made, because each baby is a law unto itself. The average of the babies in the first week of life was 120 beats per minute and that of the older babies somewhat slower. The average minimum of one three-months-old baby was about 90 beats per minute, and that of another three-months baby 100 per minute. Slight movements which were visible practically always elevated the pulse-rate 10 to 20 beats, while violent exercise, such as nursing or crying, increased the pulse-rate 50 to 60 beats. When the pulse was increased for twenty minutes, as it was during a nursing, it took about ten minutes after the exercise was finished for the pulse-rate to reach the normal. Sometimes it dropped below normal after continued exercise, and remained there for three to five minutes. The pulse, therefore, did not reach the normal line in some instances until fifteen minutes after the muscular exercise was finished.

A very close relationship was found to be established between the carbon dioxid production, the pulse-rate and the muscular movements of the infant as recorded on the smoked paper drum. In so far as possible, only those periods in which the drum indicated minimum muscular activity were used for comparison. Under these conditions the relationship between the pulse-rate and the metabolism was very apparent.

A single record will demonstrate the interesting relationships above pointed out. Record 2 with Baby 5, November 16, 1911. The baby was placed in the chamber and after some time quieted down, and the first record commenced at the point marked *I* on the curve shown herewith (Fig. 4). The first period ended and the second began at point *II*. The results are given in the following table:

BABY 5. RECORD 2. NOVEMBER 16, 1911. WEIGHT NAKED 7.6 KILOS. AGE 7½ MONTHS

Period	Thirty Minute Periods	
	Pulse per Minute	Carbon Dioxid, Gms. per 30 Min.
1	117	3.49
2	108	2.73
3	113	2.97
4	122	3.24
5	117	3.33
6	130	3.41

Accompanying this are also given two kymograph records which show the graphic movements of the baby during the periods in which the carbon dioxid excretion was determined.

Period 1 represents the time between marks *I* and *II* on the chart. A close examination of the curve will show definite rhythmical movements which are unquestionably those of respiration. It is obvious that in Period 2, that is, from *II* to *III*, there was the minimum activity, and

a comparison with the pulse-rate and carbon dioxid production shows that during this period there was the minimum pulse and the minimum carbon dioxid production. In fact, the agreement between the pulse-rate, carbon dioxid production and the graphic records on the curve is very striking. During the period from V to VI the graphic records showed a reasonably quiet period. On the other hand, during Period 5, which corresponds to this time, the carbon dioxid was slightly higher than during Period 4. This undoubtedly can be explained by the fact that the greatest activity during Period 4 was just before the end of the period, and unquestionably there was an accumulation of carbon dioxid in the chamber which was not swept out before Period 5 began. At this time residual analyses of the air in the chamber were not made, as it was found that the ventilation was sufficiently rapid to maintain the carbon dioxid content of the air at approximately .06 per cent. throughout the whole test. For extreme accuracy, it is obvious, therefore, that there should be a determination of the carbon dioxid at the end of each individual period. The excessive activity at the end of Period 6 was caused by the child's waking up and the last few minutes crying lustily.

While to the eye the child was "quiet" throughout all but the last period and apparently "absolutely quiet" in both Periods 2 and 3, the graphic records show considerably greater muscular activity during Period 3 than in Period 2, and enough to produce almost a 10 per cent. increase in the metabolism.

Although the results of our investigations on the whole are not yet ready for publication, we feel convinced of the importance of considering in all subsequent metabolism experiments the pulse-rate of the infant, and particularly the degree of muscular activity. The enormous variations in the total metabolism as affected by what might otherwise appear to be slight muscular activity, are such as to lead us to question seriously all experiments made in twenty-four periods, and we wish to assert that all metabolism experiments on infants made without known controlled pulse-rates and without graphic records of muscular activity are lessened enormously in value by the absence of these important factors.

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CONGENITAL OBSTRUCTION OF THE POSTERIOR URETHRA: REPORT OF A CASE IN A BOY AGED FIVE YEARS *

J. H. MASON KNOX, JR., M.D., AND T. P. SPRUNT, M.D.

BALTIMORE

Urethral obstruction to the urinary flow may be brought about by a number of conditions. They are for the most part the result of inflammatory processes in the urethra itself, or of pressure on its lumen by the growth of surrounding structures, notably in prostate hypertrophy.

These changes acquired after birth are of frequent occurrence and are to be sharply distinguished from obstruction of the urethra present, although perhaps unrecognized, at the time of birth.

Without other reference to the interference with the urinary flow from gross malformation of the genito-urinary tract, and to the stricture of the urethra due to occlusion or narrowing of its external orifice, or of the pars navicularis, we wish to report an instance of a form of congenital membranous obstruction occurring in the prostatic portion of the urethra, because apparently this condition has not attracted the attention, at least in this country, that it deserves, and it may be that cases which might be relieved are not recognized.

CASE REPORT

History.—The case reported concerned a boy, F. S., aged 5 years. His family history was good; his father and mother were living, five brothers and four sisters were alive and well, and had no symptoms similar to those of the patient. The birth was normal. From infancy it was noted that there was frequency of micturition. It was necessary for the patient always to wear napkins, which were wet, according to the mother's statement, "about every half hour." The urine was described as often being "thick and milk-like." Otherwise the patient's life was uneventful until 3 years of age, when he had measles. Following this illness the patient seemed susceptible to colds and had much of the time a purulent discharge from the left ear.

He first came under the observation of one of us on June 26, 1911, when at the age of 4 years, he was admitted to The Thomas Wilson Sanitarium complaining of loss of weight and strength and moderate diarrhea.

Examination.—On examination the boy was found to be sparely nourished, pale and with evidences of rickets—marked Harrison's grooves and a moderate rosary. His weight was 23 pounds. The lungs and heart were normal. The abdomen was considerably distended and pendant.

On palpation in the left lumbar region there was made out a soft movable lobulated mass extending from the anterior superior spine to the costal margin and to about midway between the umbilicus and the lateral border of the abdomen. This mass could readily be brought between the fingers in bimanual palpation; its borders were rounded and it was a little sensitive on pressure and dull on per-

* From The Thomas Wilson Sanitarium and the Medical and Pathological Departments of Johns Hopkins Hospital.

cussion. On the right flank a similar smaller mass could be made out emerging from the lower border of the liver.

A third rounded mass was detected in the mid-line extending from the symphysis pubis to the level of the umbilicus. This was oval in shape and regular in outline, freely movable and suggested an enlarged urinary bladder.

The liver was readily palpable 3 cm. below the costal margin and was not tender. The spleen was not enlarged.

External genitalia were normal. The patient had no fever and there was no history of intestinal obstruction.

Urine examination was important. The urine was slightly turbid and of low sp. gr. (1,002 to 1,004) and acid in reaction. It contained but a trace of albumin and no sugar. On microscopical examination a large number of pus cells were found, a few epithelial cells and red blood corpuscles. There were no casts. The amount of urine collected for twelve hours was 350 c.c. No tubercle bacilli were found in a centrifuged specimen. An attempt was made to catheterize the patient but the external meatus was too small to admit the smallest catheter available. There seemed to be at that time little interference with the flow of urine; no vesicle tenesmus was noted and there was no undue sensitiveness over the bladder.

A von Pirquet skin test was negative.

The urinary findings suggested a cystitis or pyelitis. The presence of the lobulated tumors above described in the flanks made the diagnosis of congenital cystic kidneys a possibility.

No marked change was noted in the patient's condition for several days, after which the lateral masses became smaller and finally could hardly be detected. Their reduction in size was apparently associated with the more thorough emptying of the bowels, although during the time of observation of more than two weeks there had been a formed or semi-formed large stool every twenty-four hours. Slight variation in the size was noted from day to day also in the fluctuating mass above the symphysis pubis.

The child's general condition bettered. His appetite was good and he was discharged improved on July 13. The clinical diagnosis at the sanitarium was: Pyelitis, hypertrophy and dilatation of bladder, rickets, intestinal indigestion with distention and partial fecal impaction.

The patient was not seen again until January, 1912, an interval of more than five months.

At this time he came to the children's out-patient department, The Johns Hopkins Hospital. He looked pale and extremely ill. The history was that although he had not been strong he had had no acute illness until two weeks before, when there had developed a cough and abdominal pain. He had since that time become progressively worse.

He was admitted to the service of Dr. Barker January 3. On examination the boy was much emaciated. The breath-sounds were harsh and accompanied by a few moist rales. The abdomen was distended and a number of soft masses thought to be intestinal coils were made out on palpation.

Above the symphysis and extending nearly to the umbilicus was the same oval mass before noted, apparently a distended bladder. The blood examination was as follows:

Red blood corpuscles.....	5,100,000
Leukocytes.....	11,000
Hemoglobin	70 per cent.

The urine contained a large number of pus cells and a trace of albumin.

There was a purulent discharge from each ear, a large abscess in the left tonsil and a mucopurulent exudate on both tonsils and the pharynx.

The Wassermann reaction was negative. The patient was given bismuth by mouth and the motility of the intestines determined by x-ray examinations.

The stomach appeared slightly distended. The motility of the small intestines seemed normal. The sigmoid flexure of the colon was displaced somewhat to the right and there seemed to be an unusual stasis between the sigmoid and the rectum.

This condition helped to account for the large lobulated mass in the left flank which gradually disappeared when the bowel was thoroughly evacuated. There was some phimosis and the patient was circumcised.

The child did not improve in the hospital. On several occasions acute dilatation of the stomach was noted and shortly before exitus on January 18, there were repeated convulsive spasms.

The temperature did not rise above 99 F., nor did the pulse exceed 120 to the minute.

PATHOLOGICAL FINDINGS

Necropsy (3670) was performed ten hours after death by Dr. Sprunt.

Anatomic Diagnosis.—Congenital malformation with obstruction of the prostatic urethra; dilatation and hypertrophy of the bladder and ureters; bilateral hydronephrosis; chronic posterior urethritis, cystitis, ureteritis and pyelitis; bilateral chronic suppurative otitis media; cloudy swelling of viscera; emaciation; unilateral congenital cystic kidney; chronic pleural adhesions; operative scar of circumcision; acute anterior urethritis; adenoma of right adrenal.

The body is that of an emaciated male child, 80 cm. in length. There is no subcutaneous edema. The prepuce has been recently removed; otherwise the external genitalia seem normal on inspection and palpation.

After opening the abdominal cavity the viscera are found normally disposed, excepting the cecum, which lies in the left lower abdominal quadrant, is quite freely movable and can easily be brought back to its usual position. The bladder is very large and extends half way to the umbilicus. By firm pressure on the bladder a very small stream of urine can be expressed from the external meatus of the urethra. On following the sigmoid flexure into the pelvis it is thought at first that it turns on itself and runs back upward toward the right kidney, but after further dissection, this structure is found to be an enormously dilated and hypertrophied ureter of about the same size as the sigmoid flexure of the colon.

Examination of the brain and meninges reveals no abnormalities. Except for pleural adhesions on the right side and a mild grade of bronchitis, the thoracic viscera are normal. The heart weighs 70 gm.

The spleen, pancreas, stomach and liver show nothing noteworthy. The adrenals are normally placed. The medulla of the left adrenal is softened. About the center of the right adrenal there is an irregular thickening, roughly 1.5 cm. in diameter, which seems fused with the kidney capsule beneath it. It resembles in general the adrenal cortex but with less regular markings and with rather coarse, white strands running through it.

The organs of the urinary system were carefully dissected and a sketch made of them *in situ* by Mr. J. T. Webster of the Johns Hopkins Medical School (Fig. 1). The kidneys are in their normal position and are both enlarged, but are not exactly alike. The larger size of the left kidney 9x4.25x3.5 cm., is only partly explained by the formalin injection of its ureter under slight pressure. On palpation the kidneys give a distinctly fluctuating sensation as if the organs were merely thick-walled sacs. The fetal lobulation is easily seen on both and on the surface of the smaller right kidney, 7x5x2.5 cm., there are several thin-walled cysts, the largest measuring 2 cm. in diameter. On longitudinal incision both kidneys consist of a mass of dilated cystic spaces, evidently the dilated calyces which are continuous with the ureter below. The whole thickness of the kidney parenchyma, from calyx to capsule, averages from 5 to 7 mm. with occasional thicker areas, measuring 15 mm. between the larger calyces. The structure of cortex and medulla cannot be distinguished. The blood-supply of the kidneys seems quite normal.

The ureters show the normal relationship to kidneys and vessels; they are very tortuous in their course but otherwise follow the normal path. They are greatly enlarged, of the same size, 1.5 cm. in diameter, and have firm, thick walls.

The bladder was opened longitudinally along its anterior wall while *in situ*. It measures 7 cm. in length from internal meatus to apex. There are scattered ecchymoses in the mucosa which is elsewhere quite pale. Beneath the mucosa the musculature is thrown up into very prominent trabeculae. The ureteral and urethral orifices are in their usual relative positions. A small probe is easily passed into the ureters from the bladder, but in the urethra meets with an obstruction in the lower prostatic portion. Similarly when the urethra is sounded through the external meatus, an obstruction is encountered in the same region. The whole urinary tract is then removed *en masse*, including half of the anterior urethra and opened along the anterior wall.

Through the wide internal meatus the bladder becomes continuous with the greatly dilated and thick walled prostatic urethra which forms an oval sac with the distal, blind extremity 2.5 cm. from the internal meatus. The floor of this pouch shows several prominent folds near the midline which end below in an unusually prominent verumontanum which reaches three-fifths of the distance from the internal meatus to the blind end of the sac. The opening of the vagina masculina is conspicuous, shaped like a crescent, with the concavity directed upward. Numerous orifices of the prostatic ducts are observed on each side of the verumontanum but those of the ejaculatory ducts are not seen. Immediately below the verumontanum, the ridge, of which it forms a part, divides into two prominent diverging folds which soon fuse with the anterior wall of the urethra instead of fading out gradually on the posterior wall of the membranous urethra as usual. Just below the verumontanum between the diverging folds, there is a small equilateral triangular opening whose sides measure about 3 mm. A probe passed through from the anterior urethra presents in this opening and abuts against the hypertrophied verumontanum. This is the only communication between the anterior and posterior portions of the urethra.

The mucosa of the dilated prostatic urethra is pale and resembles that of the bladder in appearance. The mucosa of all that portion of the urethra anterior to the obstruction is swollen, reddened and shows small ecchymoses.

The anus and rectum seem quite normal. Nothing unusual is noted about the seminal vesicles or vasa deferentia.

MICROSCOPIC DESCRIPTION

Urethra: Sections were prepared from the lower end of the prostatic sac; through the folds immediately below the verumontanum; through the distal portion of the verumontanum; and through the proximal end of the same structure. The blind end of the prostatic urethra is clothed with stratified pavement epithelium similar to that of the esophagus. The folds below the verumontanum are covered with the same type of epithelium but that of the anterior urethra is so badly desquamated that its nature cannot be definitely determined. Over the verumontanum and the rest of the prostatic urethra, the usual type of epithelium is present. The subepithelial tissues everywhere consist of a very dense, fibrous tissue with few elastic elements. Small clusters of mononuclear cells may be found occasionally beneath the epithelium. The vagina masculina is not prominent. Indeed, it is less conspicuous than is often the case.

Bladder: The bladder wall is thick, the muscle bundles large. The mucosa shows scattered mononuclear cells. The epithelium of the mucosa is not preserved.

Ureter: The ureter, also, is greatly thickened and contains many elastic fibers. The epithelium is of the normal type and very well preserved.

Kidney (Fig. 2): Examination under a dissecting lens reveals the whole width of kidney parenchyma much narrowed. The medullary portion is no longer pyramidal in shape but is flattened out, the tubules running almost parallel with the

lining of the dilated calyces. The tubules of the cortex are enormously enlarged being quite prominent even under the power of the dissecting microscope. With higher power the epithelium of the pelvis is found well preserved. Beneath it the mucosa is infiltrated with plasma cells and contains no elastic elements. The connective tissue between the straight tubules in the medulla is thickened and contains scattered mononuclear cells. The walls of the larger blood-vessels are thickened. This is especially true of the intima. The capsule of the kidney is considerably thickened and extending down from it in places may be seen strands of connective tissue. Between these connective tissue strands the tubules are markedly hypertrophied with wide lumina and very large cubical or flattened granular cells, whose nuclei stain well. The lumen of each tubule contains a foamy material and occasionally a hyaline cast. The glomeruli are few in number, but those present seem very nearly normal. Here and there one which is imbedded in a connective tissue strand is entirely hyaline or shows some hyaline change.

Sections from other organs show nothing of interest in this connection, save, perhaps, those from the right adrenal. The tumor-like nodules consist of large nests of epithelial cells separated by connective tissue trabeculae, some of which are extensively calcified. The appearance and arrangement of the cells is strongly suggestive of the normal adrenal cortex. The cells, however, contain practically no fat or lipoid substances.

SUMMARY OF CASE

In summary, we present the case of a boy 5 years old, who had had difficulty in controlling micturition from infancy. Urine passed every half hour of day and night, and was attended by no pain.

Four weeks before death there occurred a sudden onset of the terminal illness with cough, abdominal pain, vomiting and constipation. Physical examination showed malnutrition, purulent conjunctivitis, discharge from left ear, tonsillar abscess, protuberant abdomen, a tumor above the symphysis, with dull percussion note, redundant foreskin with phimosis; hemoglobin 70 per cent. There was no fever. Later vomiting became frequent, there were many convulsive attacks and breathing suggestive of air hunger. He was circumcised three weeks before death with the result of slightly improving the flow of urine. Attempt at catheterization failed.

At autopsy there was found an obstruction in the prostatic portion of the urethra, which was converted into a blind pouch by the fusion of its anterior and posterior walls, due apparently to an overdevelopment of folds normally present immediately distal to the verumontanum. A small triangular opening whose sides measured 3 mm. situated in the floor of this pouch was the only communication with the anterior urethra and through this the urine must pass. As a result of the urinary stasis there had occurred marked dilatation and hypertrophy of bladder, ureters and kidney pelves with typical hydronephrosis terminating in uremia.

Aside from the condition in the urethra, no other congenital anomaly was discovered unless the adrenal adenoma may be so considered.

INCIDENCE OF CONGENITAL URETHRAL OBSTRUCTION

While the condition here described and other types of congenital urethral obstruction cannot be considered of frequent occurrence, neither

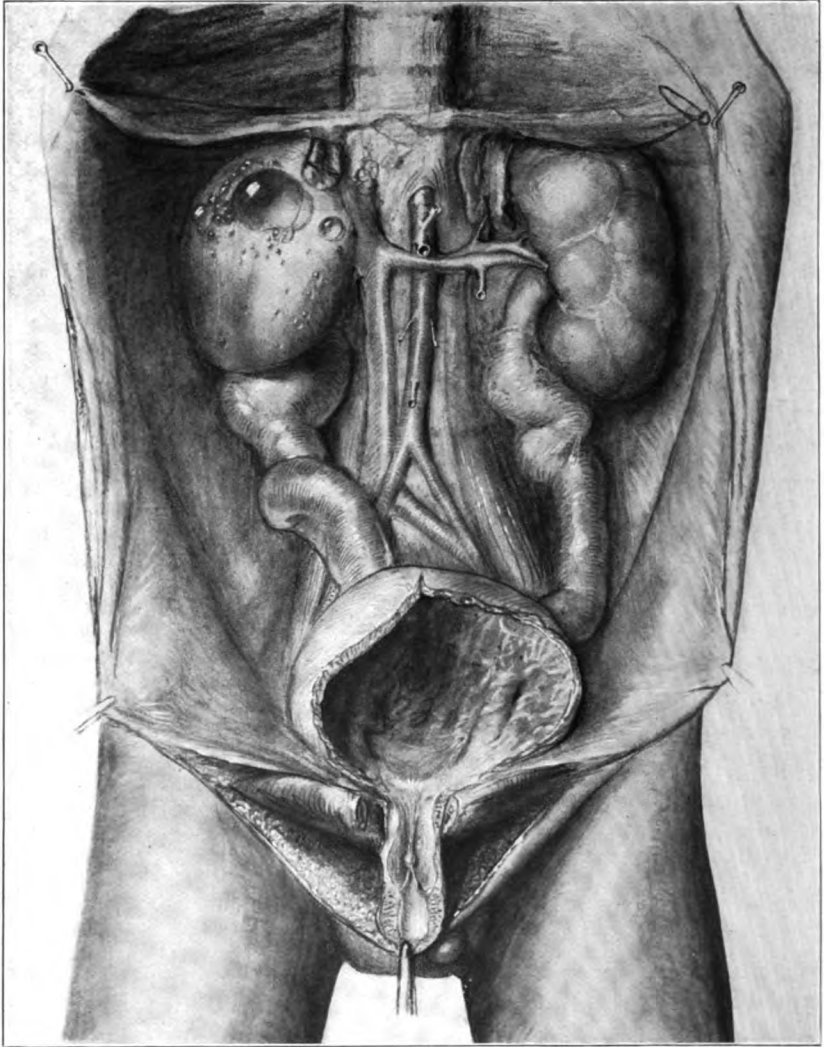


Fig. 1.—Drawing at autopsy by T. J. Webster. Note the enlarged, lobulated cystic kidneys, the enormously dilated and tortuous ureters; the hypertrophied, distended bladder and the hypertrophied membranous folds in the prostatic urethra constituting the obstruction to the urinary flow.

are they excessively rare and we feel, after reviewing the literature, that they may be met with more frequently than is generally supposed.

Very similar cases, some of them almost identical with ours, are reported by Wilckens,¹ Lederer,² Tolmatschew,³ Bednar,⁴ Godart,⁵ Budd,⁶ Velpeau,⁷ Schlagenhauser,⁸ Commandeur,⁹ Bonnet,¹⁰ Reboul,¹¹ Fuchs,¹² Porak,¹³ Lindeman,¹⁴ Picard.¹⁵ In addition Bazy¹⁶ reports six cases, in older boys and in men, which he had observed clinically, as cases of congenital stricture in the region of the pars membranacea or pars bulbosa and emphasizes the importance of congenital strictures of the urethra even in adults. Ebert¹⁷ reports a similar clinical case in which he punctured the obstructing membrane and discharged his patient as cured. There are numerous other reports of congenital stricture in the anterior urethra, due to valvelike structures, partial or total occlusion of the urethra throughout a smaller or greater portion of its extent, atresia of the external meatus, etc. Englisch,¹⁸ in a recent exhaustive article, has collected a large number of cases of congenital narrowing of the male urethra.

Most of the published observations similar to the case here recorded occurred in new-born children, or babies a few days or weeks old. A number, however, have been observed in older children, in whom the lesions seem to have remained latent for a time and then gradually became

1. Wilckens: Zur Frage der kongenitalen Stenosen der männlichen Harnröhre. *Ztschr. f. Urol.*, 1910, iv, 814.

2. Lederer: Ueber eine angeborene membranöse Verengung der Pars prostatica urethræ. *Arch. f. path. Anat. u. Physiol.*, Berl., 1911, cciii, 240.

3. Tolmatschew: Ein Fall von semilunaren Klappen der männlichen Harnröhre und von vergrößerter Vesicula prostatica. *Arch. f. path. Anat. u. Physiol.* Berl., 1870, xlix, 348.

4. Bednar: Quoted from Wilckens,¹ Lindeman,¹⁴ et al.

5. Godart: Valvule anormale dans le canal l'urètre. *Bull. Soc. anat. de Paris*, 1854, xxix, 137.

6. Budd: Quoted from Wilckens,¹ Lindeman¹⁴ et al.

7. Velpeau: *Traité d'anatomie chirurgicale*, Paris, 1826, ii, 297.

8. Schlagenhauser: Ein Beitrag zu den angeborenen Klappenbildungen im Bereiche der Pars prostatica urethræ. *Wien. klin. Wchnschr.*, 1896, No. 15, p. 268.

9. Commandeur: Dilatation de l'appareil urinaire chez le fœtus par rétrécissement valvulaire congénital de l'urètre. *Lyon méd.*, 1898 Mars. 13.

10. Bonnet: Quoted from Wilckens.¹

11. Reboul: Quoted from Wilckens.¹

12. Fuchs: Zwei Fälle von kongenitaler Hydronephrose. *Inaug. Dis.*, Zurich, 1900.

13. Porak: Quoted from Commandeur and Lederer.⁹

14. Lindeman: Casuistischer Beitrag zur Frage der angeborenen klappenförmigen Verengung der Pars prostatica urethræ. *Inaug. Dis.*, Jena, 1904.

15. Picard: Convulsions à forme eclamptique chez un homme, *Gaz. méd. de Strassburg*, 1855, No. 7, p. 259. Quoted from Lindeman.¹⁴

16. Bazy: Rétrécissement congénital de l'urètre chez l'homme. *Presse méd.*, 1903, p. 215.

17. Ebert: Quoted from Segall. Ein Fall von angeborener Harnröhrenverengung. *Inaug. Dis.*, Königsberg, 1890.

18. Englisch: Ueber angeborene Verengungen der männlichen Harnröhre. *Folia urologica*, 1909, iv and v.

more severe. Budd's patient was 16 years old, Lederer's 11, Wilckens' $2\frac{1}{4}$, our one case 5. Picard regarded the valve-like lesion in his 40-years-old patient as of congenital origin. The symptoms are dated in three of these cases from an attack of one of the acute infections.

SYMPTOMATOLOGY

Of the instances observed in older children, the case here reported is quite typical if we accept those symptoms due to the local infections in the middle ear, tonsils, etc. In the new-born infants and babies a few



Fig. 2.—Section of kidney under low power. The glomeruli appear normal; tubules of cortex are greatly dilated; tubules of medullary portion are compressed and run parallel to lining of dilated calyces.

days old the symptoms are of course simpler and consist in the extreme cases of failure to pass any urine whatever.

PATHOLOGY

Englisch¹⁹ divides all congenital obstructions in the urinary passages of children into two great groups:

- A. Obstructions which exist in embryonic life, but later disappear.
- B. Obstructions which remain permanently.

19. Englisch: Quoted from Wilckens.¹

Under Group "A" he includes the fusion of epithelial folds in the ureters; a similarly produced atresia of the ureteral opening into the bladder; valve formation and kinkings of the ureters which disappear with subsequent growth; atresia of the internal or of the external meatus of the urethra; atresia of the prepuce; and finally atresia of the orifices of the utriculus masculinus and of Cowper's glands.

Under Group "B" are found the valves and stenoses. The valves occur at the transition between ureters and kidney pelvis, rarely in the bladder; especially in the prostatic part of the urethra at the upper and lower ends of the colliculus seminalis; in the anterior urethra at the end of the fossa navicularis, at the external meatus and even in the foreskin.

The places of predilection of the stenoses in the urethra are especially the point of union of the pars membranacea with the pars bulbosa, the posterior end of the fossa navicularis and the external urethral orifice.

The folds or valvelike obstructions in which we have been most interested seem to occur in those regions where folds or ridges are normally found in the urethral mucosa; and this is especially true of the anterior end of the colliculus seminalis where most of these obstructions are encountered. Here in the normal urethra there is a division of the crista urethralis into two ridges which, becoming less and less prominent, gradually fade out in the posterior wall of the bulbous urethra.

In most of the reported cases of obstruction at this point, the lesion seems to have been produced by an overdevelopment of these folds which fuse with the anterior wall with the formation of membranes extending across the urethral lumen. The resulting structures vary slightly in individual cases. Schlagenhauser describes the obstruction in his case as due to a funnel-shaped valvular occlusion. In others the pressure of the urine has resulted in a more definite pouch, with this concavity of the membranes directed backward toward the bladder. The size and relationships of the opening through the obstruction vary also, and this is of considerable practical importance in the clinical examination. A sound introduced into the urethra may pass quite unhindered into the bladder, as in the case reported by Bednar, or the opening may be so small and so situated immediately below an enlarged verumontanum, as in our own case, that the smallest catheter is obstructed.

Budd, Godart and others compare the obstructing membrane to the valves of a vein or to the semilunar valves of the heart. In these cases no interference is offered to the passage of an instrument from below.

The secondary pathologic changes are quite uniform in kind, differing only to a certain extent in degree. There is invariably dilatation and hypertrophy of the higher urinary passages with bilateral hydronephrosis.

Histologic examination shows a metaplasia of the epithelium in the posterior urethra from the usual transitional type to a stratified squamous type like that of the epidermis.

GENESIS

The occurrence in young children and the similarity of the pathologic anatomic pictures in different cases establish the lesion as congenital and suggest strongly that it has its origin in some slight variation from the normal in the course of development. It must then be through study of the embryology of this region that we shall finally arrive at a satisfactory explanation for these anomalies. At present this is not to be found.

Certain forms of obstruction in the prostatic urethra have a ready explanation in the present state of our knowledge of embryology. Those due to the abnormal persistence of Müller's ducts in the male come under this class. In an over-development of the sacculus prostaticus, the homologue of the vagina, this structure may become so large that it is pushed out into the urethra and may block the flow of urine. The outer genitalia may show no abnormality.

Again, in analogy to the "hymen imperforatus" in women, the sacculus prostaticus, utriculus prostaticus, or vagina masculina, as it is variously named, may be closed at its urethral end. This may be associated with a cystic widening of the utricle which leads to urine retention. Such lesions are attributable to more or less slight degrees of pseudo-hermaphroditism.

Concerning the development of the folds in the mucosa constituting the crista urethræ, we have been able to find little or nothing. We do not know what the relationship is, if indeed there is any, between these folds and the prostatic utricle, the remains of Müller's ducts. They are said to bear some relationship to the developing prostate gland.²⁰

Two principle views are presented in the literature by students of these cases. One of these is that the abnormality is due to an over-development of folds normally present in the mucosa, and no explanation is attempted of the initial stimulus to growth. Englisch is of the opinion that after the establishment of a certain grade of obstruction, the pressure of the urine exerts a continuous irritation on this region with the stimulation of epithelial growth and production of proliferative inflammatory changes which account for the gradual increase in the efficiency of the obstruction and in the gravity of the symptoms.

Posner,²¹ Wilckens and especially Lederer are inclined to regard this lesion as a malformation due to arrested development. Lederer says in favor of this view that it occurs at about the point of union between the entodermal and ectodermal portions of the urethra.

Recent workers in human embryology are at variance in their views on the development of the urethral canal. Felix,²² who writes the

20. Lowsley: Personal communication (Article in press). *Am. Jour. Anat.*, June 15, 1912.

21. Posner: Ueber angeborene Stricturen der Harnröhre. *Berl. klin. Wehnschr.*, 1907, xliv, 275.

22. Felix: Die Entwicklung der Harn- und Geschlechtsorgane. *Handbuch der Entwicklungsgeschichte des Menschen*. (F. Keibel and F. P. Mall), ii, 732.

exhaustive article on the development of the urinary and sexual organs in Keibel and Mall's system of Human Embryology, insists that the whole canal from the verumontanum to the sulcus coronarius glandis is developed from the sinus urogenitalis and is of entodermal origin. Broman,²³ on the other hand, in his recent work accepts the view that the corpus cavernosa urethræ is developed from the ectodermal or cloacal plate. Certainly this latter view would furnish the better explanation for the numerous anomalies occurring in the membranous and anterior portions of the urethra, including, perhaps, such valve-like structures as those described by Posner at the junction of the pars membranacea and the pars bulbosa. But even should we adhere to this view, the lesion we have described in the posterior urethra, is too far posterior to be ascribed to a failure in the union of entodermal and ectodermal structures. In the lack of definite knowledge we lean rather to the view that we are dealing with a simple progressive malformation and not one due to arrest of development. Certainly, the region in which this anomaly occurs is one of complex development, being the point of union of the prostatic urethra developing from the mesodermal wolffian ducts, the urethra distal to the verumontanum derived from the entodermal sinus urogenitalis, the prostatic utricle representing the remnants of Müller's ducts and the ejaculatory ducts.

CONCLUSIONS

We have been able to find no case of congenital membranous obstruction occurring in the prostatic urethra reported in full in our American literature and yet the condition has not been infrequently described abroad.

We believe that the possibility of interference with the urinary flow from such a congenital malformation should be considered whenever the cause of the obstruction is not obvious; especially should there be a persistently distended bladder. A partial obstruction of this nature is compatible with the passage of a normal daily amount of urine, but there may be either increased frequency of micturition or incontinence if the lumen is not absolutely occluded.

The condition if recognized in most instances could be easily corrected.

Autopsy findings should not be considered complete without incision through the anterior urethral wall and inspection of the complicated structures in or near the pars prostaticus.

We wish to thank Dr. Llewellys F. Barker for the privilege of reporting the case from his wards, and Mr. J. P. Webster for the excellent drawing.

23. Broman: Normale und abnorme Entwicklung des Menschen. Wiesbaden, 1911 (J. F. Bergmann), p. 476.

SUMMER DIARRHEA — HEAT — HUMIDITY *

LAWRENCE T. ROYSTER, M.D.

NORFOLK

With a literature already overcrowded with the various causes, both scientific and practical, of infant diarrhea, especially during the heated term, one is tempted to commence a paper of this character with an apology. And yet I feel that any fact which may either prove or disprove existing theories, should be set forth for the possible aid it may render other investigators along the same line.

For many years past the digestive disturbances of infants have occupied more space in our researches than all other conditions combined, and, although much has been gained and chronicled by these researches, I may safely say that up to the present moment no really definite conclusions have been reached. During all these years a large number of careful and capable students have conducted investigations on this subject, leaving in their trail almost as many theories as there were investigators, but from among all these, three have gained the most prominence, namely, milk decomposition, bacterial infection and summer heat. Two of these theories, namely, milk decomposition and bacterial infection, have been partially, if not completely, disproved as the main cause of summer diarrhea in infants, based on investigations with which you are all too familiar for me to review on this occasion. I shall therefore confine my remarks to the influence of heat, and the possible combination of humidity.

HEAT AND HUMIDITY

In looking over a vast number of statistics, gathered from all parts of the country, there has been evident a great decrease in mortality in some cities, following a pure-milk crusade, but in this instance the fact is clearly shown that prior to such a crusade the infant death-rate was much higher than could be accounted for by climatic conditions; hence these cities can only be considered statistically since the time of the institution of milk regulation.

Taking up the question, therefore, in its relation to climatic conditions, notably heat and humidity, leaving out of consideration all other factors, we find, in brief, that our observations lead to the following superficial conclusions; that infant diarrhea, as it is commonly understood, exists practically entirely in the temperate regions, is exceedingly

*Read in the Section on Diseases of Children of the American Medical Association at the Sixty-Third Annual Session, at Atlantic City, June, 1912.

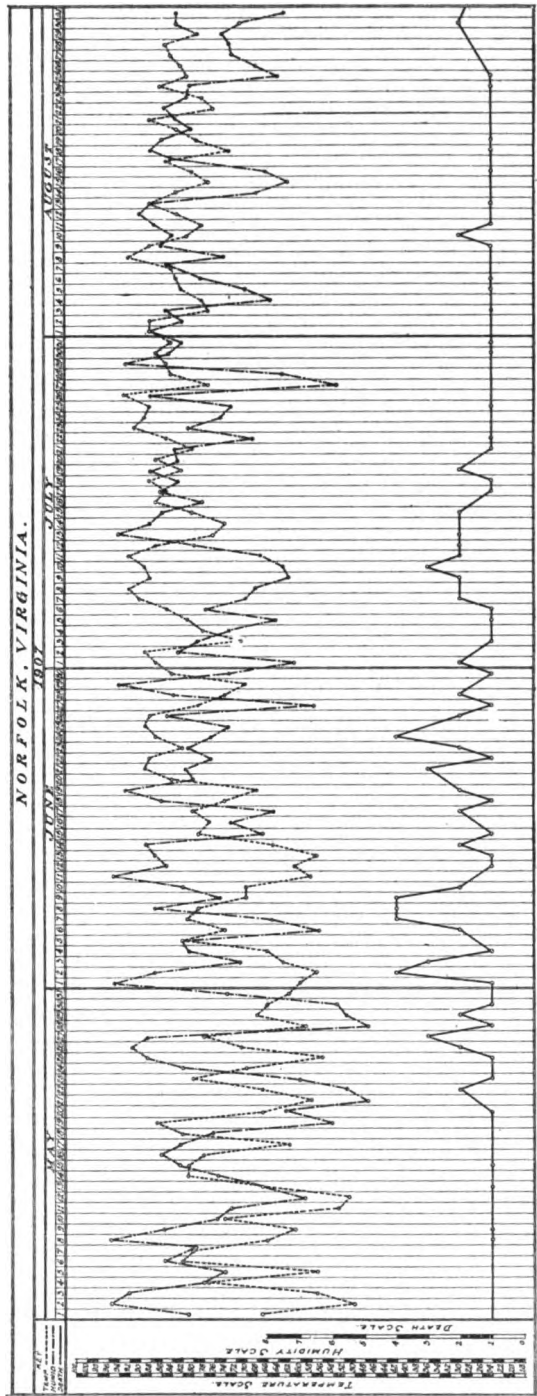


Chart 1.—Temperature, humidity and death curves in Norfolk for the months of May, June, July and August, 1907.

rare in Canada and similar countries, and equally rare in the tropics and subtropics.

The exhaustive researches of Liefmann and Lindemann, covering a period of fifteen years of daily observation in the city of Berlin, show that the death-curve, and also the sick-curve, follow an almost exactly parallel line with the 2 p. m. temperature curve. That however much the temperature may vary during the day, from early morning to late at night, the most constant guide is the 2 p. m. temperature, with which the death-curve, as I have stated, runs almost parallel. We observe, further, that in the poorer sections of the city particularly, mortality is higher among children who are deprived of out-door air; that country children are notably less affected than city children, in spite of the frequently higher temperature in the country, and that children sent to the country suffering with the condition frequently recover and recuperate very much more rapidly than those who still have to dwell in the city. Again, wherever the seaside resorts are used, or floating hospitals for the benefit of sick children, the picture is a familiar one — with what rapidity they recover and recuperate here, although the seashore may be just as hot as the city, and frequently even more humid.

It is well known that frequent bathing in cold water during the hot days, and frequent small draughts of water administered to the child, go a long way toward the prevention of summer diarrhea. And in the case of seashore and country a breeze is usually present in spite of the heat. Almost without any further argument therefore, it will be seen from these brief facts that the question largely resolves itself into one of radiation, rather than the actual instance of heat itself.

The discussion following Dr. Abt's paper at Los Angeles last year, during which remarkable statements were made by some of our friends of the far West, decided me in looking into the question of radiation still further, with the possible effect of the combination of humidity along with the heat. This latter in spite of the fact that Liefmann and Lindemann found no relation whatever between infant mortality and humidity, although they considered any humidity above 50 per cent. to be high; whereas we have very few sections of our country where the humidity is ever below 50 per cent.

There are many difficulties which present themselves in an undertaking of this kind. In studying American cities many of them are so new that records of death-rate have been kept for such a short time and are so imperfect that practically no deductions can be drawn from them. And, too, in many instances the United States Weather Bureau had been established too short a time to aid in this comparison. For no record, unless a daily one of temperature, humidity and death-rate, can give us even an approximate idea of the relations of these factors. As we

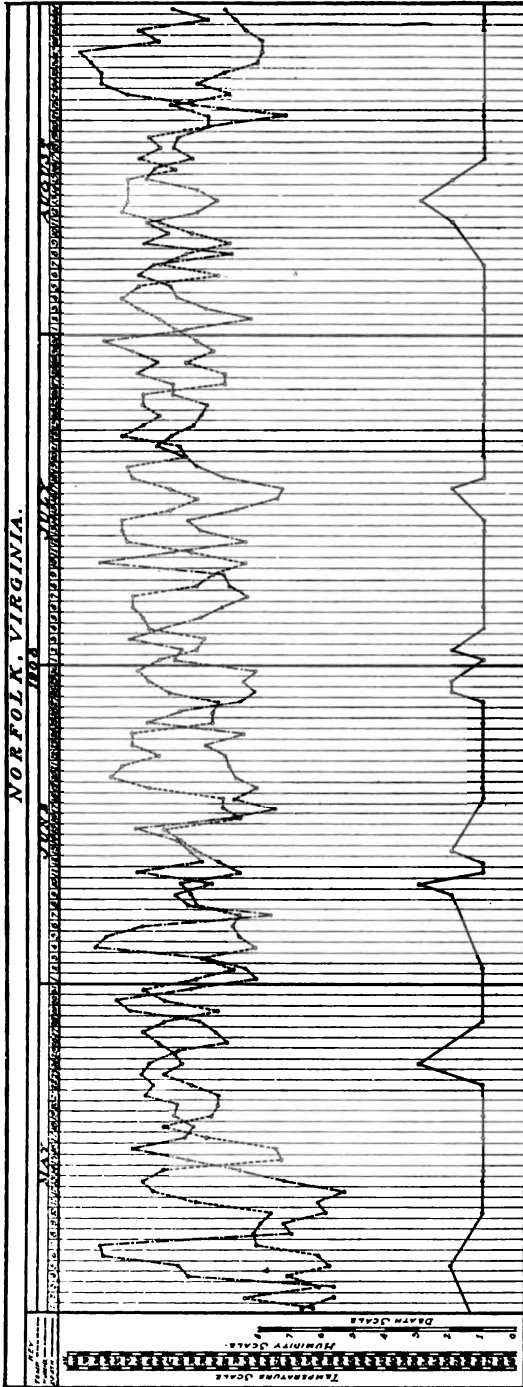


Chart 2.—Temperature, humidity and death curves in Norfolk for the months of May, June, July and August, 1908.

progress in our studies, difficulties multiply. The temperature varies in different parts of the same city, frequently as much as five, or even seven degrees, as has been shown by the German investigators above quoted, who took observations from several parts of the city, showing that in the thickly populated parts of the city the temperature was, of course, very much higher than in the suburbs, and the official weather bureau observation is always somewhat lower than that at the street level, or in other parts of the city.

The greatest difficulty in this study, however, arises from the difference between the temperature of out-of-doors and that within the dwellings, which latter is almost invariably higher, and especially in the room which, among the poor, is used as a living room and kitchen combined, where the temperature has been found to be as much as ten degrees higher than outside, thereby giving almost no possibility of radiation. Moreover, in instances where the maximum temperature in the city is registered perhaps at 2 or 3 o'clock in the afternoon, the maximum temperature in the dwellings is almost always higher during the night hours, sometimes at 8 p. m., in other instances as late as 3 the next morning. This latter emphasizes the importance of not bundling up the child too closely when it is put to bed at night, judging the necessity for bed clothing by the temperature outside of the house.

The variety of these difficulties therefore renders accurate scientific observation on the effects of climatic changes on the condition before us almost impossible. Again, the death-curve hardly gives us a fair conception of this relation, but rather would the sick-curve help us more, which, especially among the poor, where careful histories are difficult to obtain, it is practically impossible to secure. For example, where there are several sudden ascents of temperature, giving marked pinnacles in our curve, and separated by one or more days of comparatively lower temperature, it is impossible to state definitely whether the number of deaths immediately following one of these pinnacles is in reality due to the immediately preceding elevation of temperature, or to the more distant preceding one, during which the child became ill, but survived until the second or third sudden ascent immediately caused its death. These sudden rises in temperature occur more frequently during the early part of the summer, than in mid-summer, when we have a more uniform elevation of temperature. In this case the effect of the heat is rather a cumulative one, almost analogous to the cumulative effect of certain drugs. Moreover, there may develop a subacute or subchronic condition of impaired health, which the child may resist for weeks or even months, finally dying in the late summer or early autumn, in which instance the death should, in reality, be attributed to the heat of a far-preceding period. This is particularly noticeable in Norfolk, where

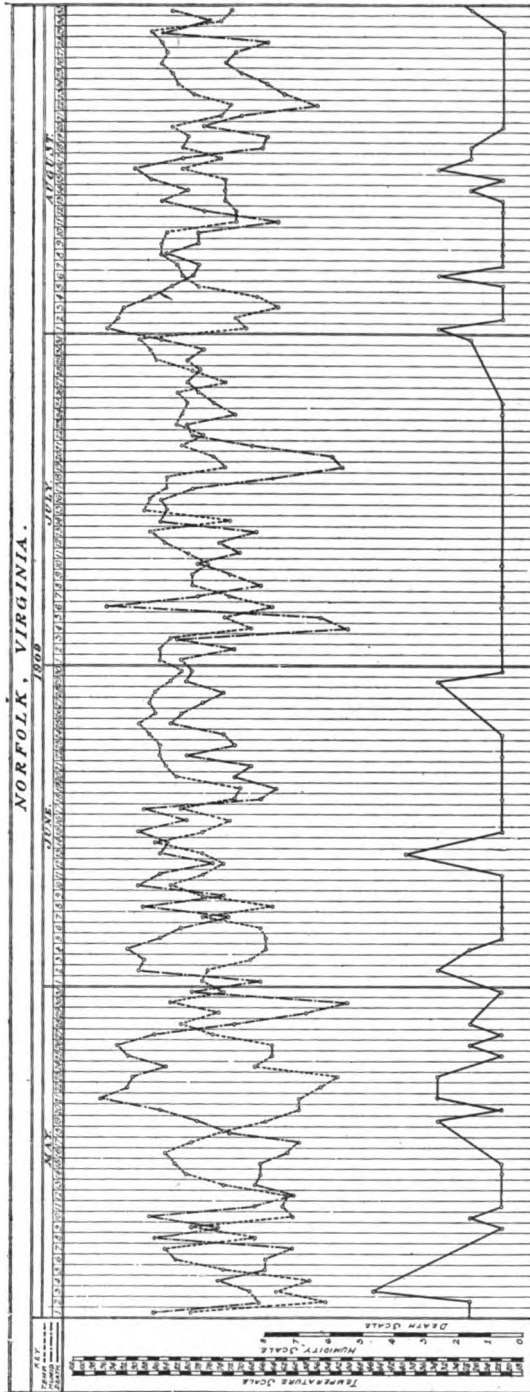


Chart 3.—Temperature, humidity and death curves in Norfolk for the months of May, June, July and August, 1909.

the large number of deaths from summer diarrhea during the early heat periods occur among the negroes, while the death-rate in the late summer shows a greater mortality among the whites. This is easily accounted for by several facts, notably the surroundings of the whites and blacks, and the superior resistance of the white stock in our city. For example, the negroes die almost as soon as they are attacked, while the whites frequently drop into a subacute or chronic state, resisting the disease for a longer period, due largely to the more intelligent care, but finally succumbing at a later period.

Considering, however, all of the difficulties, the fact is that we are at present nearer to the conception which Meinert announced to us in 1881 on heat stroke, not that the heat alone is the cause, but the heat is undoubtedly the precipitating cause, and other factors are back of it, notably the effect of artificial feeding, as among artificially-fed children the vast majority of these cases are found. The digestion of the artificially-fed child is usually taxed to its utmost by a food at best only poorly suited to its digestive powers, and no doubt the heat or lack of radiation merely precipitates the fatal condition.

In order, therefore, to investigate even superficially this question, I have gathered data from as many cities in the United States as was possible. In every instance, except that of Norfolk, I was able only to get monthly averages. Hence the curves show us comparatively little concise data. The general averages themselves are, however, exceedingly interesting. In some instances they uphold the relation between humidity and temperature, and in others they tend to disprove it. The death-rate in the following tables is for gastro-enteritis in children under 2 years of age. Taking Boston as a representative eastern city, though somewhat north of the real temperate zone, we find the following:

Boston:
Population 670,585.
Mean maximum temperature 58.
Mean minimum 42.
Average temperature 50.
Humidity 71.
Death per thousand .92.

Even a death-rate thus calculated is misleading, because the only accurate census that can be secured is that of 1910. And on this census these rates are based, because the estimated census per year is notably inaccurate. For example:

Birmingham, Alabama:
Population 132,685.
Mean temperature 63.7.
Mean humidity 78.6.
Death-rate 1.

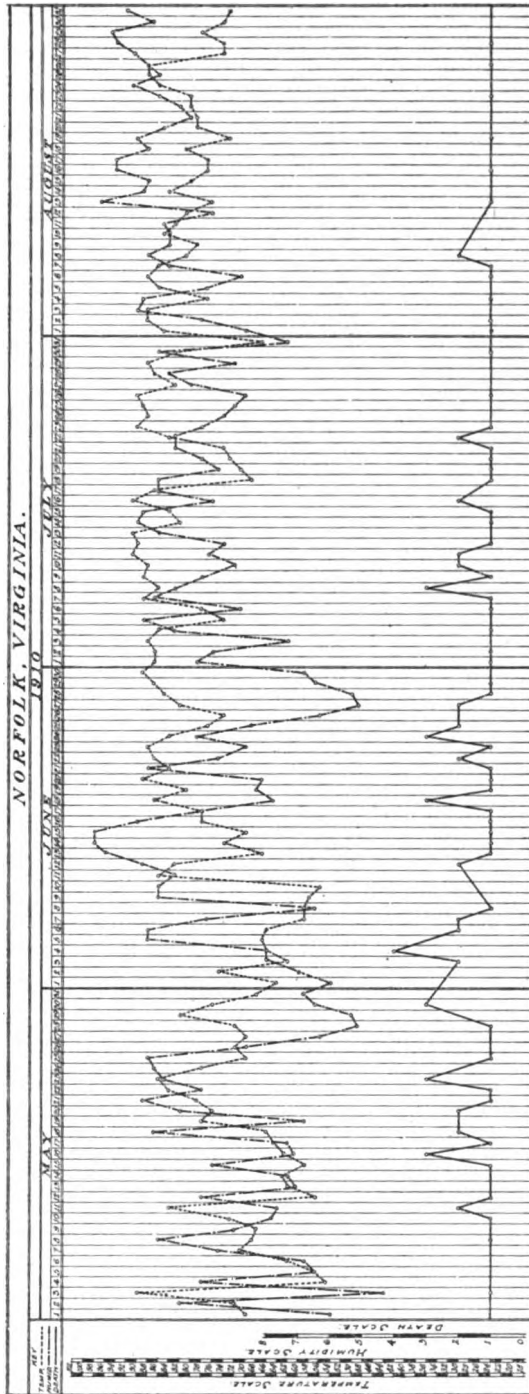


Chart 4.—Temperature, humidity and death curves in Norfolk for the months of May, June, July and August, 1910.

This is the death-rate when based on the 1910 census, but if based on the average yearly census we have a death-rate of 1.38, which is, in all probability, more nearly accurate.

Chicago, Ill.:

Population 2,185,283.

Mean temperature 50.

Mean humidity 76.

Death-rate per thousand 1.2.

Of course this does not show up clearly the sudden changes of both temperature and humidity which are known to occur in Chicago.

San Francisco:

Population 316,912.

Mean humidity 75.7.

Mean temperature 55. More or less uniform throughout the year, with practically no sudden changes. Death-rate per thousand .30.

Cleveland, Ohio:

Population 560,663.

Mean temperature 49.4.

Mean humidity 72.3.

Death-rate 1.02.

Practically all of the deaths of the year occur during July, August and September, with August as the highest point. Again this shows comparatively little, because daily records could not be secured.

Now Orleans gives us the greatest problem of all cities, as has been long recognized, the deaths here occurring on the up-grade of temperature, and not at the height as in other cities, occurring in April, which is very different from any other American city. The humidity is very nearly uniform throughout the whole year.

New Orleans:

Mean humidity 78.

Mean temperature 70.

Death-rate 1.27.

Turning, however, to San Antonio, we have a remarkable record.

San Antonio:

Population 96,000.

Maximum mean temperature 87.9.

Minimum mean temperature 52.1.

Average annual temperature 70.

Mean humidity 67.

Death-rate .49.

The temperature in San Antonio frequently reaches for an average of a whole month considerably over 100, humidity more or less uniformly low and even, and practically no exacerbation in the death-curve, with the single exception of May, 1910, for which there was no apparent cause.

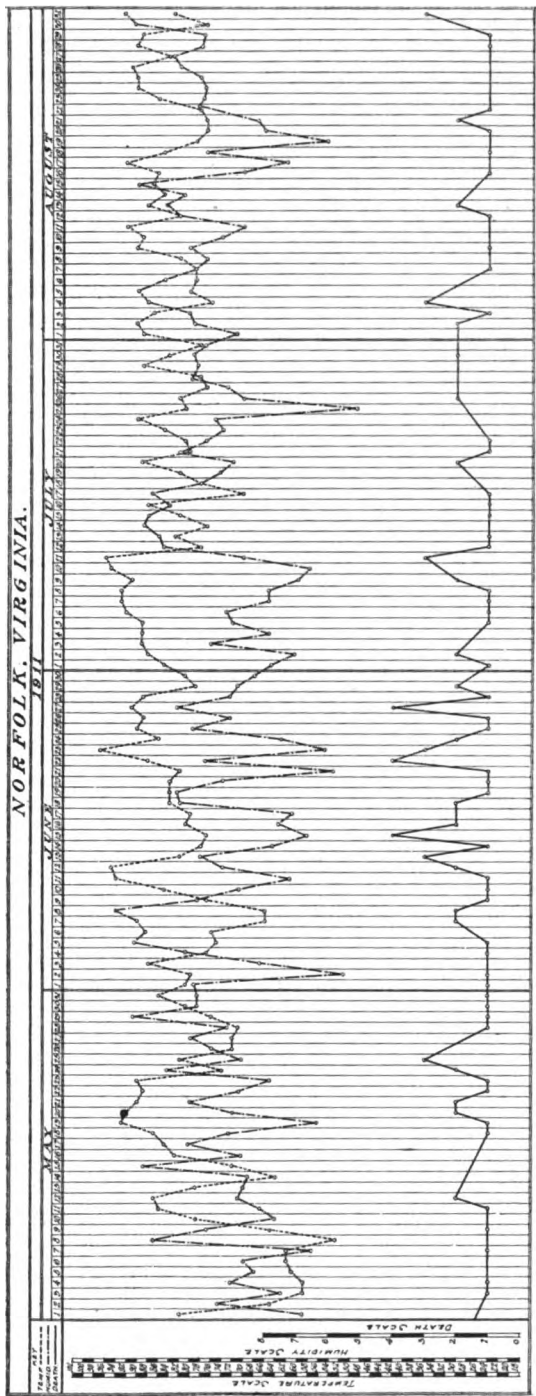


Chart 5.—Temperature, humidity and death curves in Norfolk for the months of May, June, July and August, 1911.

Denver:

Population 213,281.

Death-rate per thousand .43.

Climatic conditions are interesting.

Maximum mean temperature 63.9.

Minimum mean temperature 37.9.

Average temperature 50.9.

Mean humidity 52.3.

In Phoenix, Ariz., the statistics are drawn from a population of about 20,000. The death-rate is .60. Average maximum temperature 86, minimum 57. Humidity, 46.2. The humidity for November, December and January is rather high, which brings up the average as high as it is. The average for the rest of the year is about 35.

These records are merely interesting statistically, and give us no accurate information about the influence of sudden rises in temperature or humidity. I have, however, worked out for Norfolk a daily scale of humidity, temperature and death-rate (Charts 1 to 5) for a period of five years, and think we have a few interesting observations from this record.

Norfolk:

Population 81,000.

Death-rate per thousand 1.7.

Mean temperature 64.7.

Mean humidity 75.

The largest number of deaths in Norfolk on a single day is five, which occurred only once. A high death-rate is usually considered to be four, while two and three is about the average for high mortality. In the majority of instances where an unusual number of deaths occurs, the temperature and humidity are both well above the average, and run more or less uniformly parallel. Wherever we have an unusual number of deaths occurring on a day on which the humidity is low, we invariably have a temperature unusually high. A few examples will suffice to show these changes.

May 27, 1907, there occurred three deaths, really the first pinnacle in the curve of that year, and on this day the humidity reached 90 and the temperature 78. There was an immediate drop in the humidity, which lasted for several days, and on June 2, the death-curve reached four, while the temperature was only 57, but the humidity was 87, preceded on June 1 by humidity of 95. In this city we would hardly consider a temperature of 57 as dangerous, but the complementary relation of humidity shows up strikingly. During the next three or four days the humidity goes down to 57, while the temperature ascends rapidly to 82. The temperature remains comparatively high for the next three days, coming down on the fourth day, while the humidity again mounts to 87, during which period there are four deaths a day, again, I think, showing

a striking relation between humidity and death-rate. On June 20 the temperature reaches 84, humidity 69, with three deaths, and temperature still keeping high, humidity declining somewhat; the next pinnacle of deaths, on June 24, shows four again, illustrating the fact that although the humidity falls considerably, the temperature has soared to an unusual height. For the next several days the death-rate varies from one to two per day, until we reach July 11, when it reaches three, with a humidity of 61, unusually low for this season of the year; but on this day the temperature reaches the almost phenomenal point of 92. By this time the bulk of the mortality for our city is past, and whereas the humidity and temperature both run almost parallel, the death-rate is not particularly marked.

In the year 1908 we have only three striking pinnacles in our death curve: One on May 24, three deaths, when humidity and temperature were both high; one on June 11, with a similar condition, and one August 13, when the same number of deaths occurred, with a humidity of 76, and an unusual temperature of 92.

In May, 1909, we have the most striking pinnacle in our series. On May 3 we have five deaths, with a humidity of 69 and temperature of 66, but for the two days preceding this we have a temperature of 81 and a humidity of 86.

June 4, 1910, we have a death-rate reaching four, while the temperature reaches only 67, but the humidity reaches 89.

The only striking pinnacle in the Norfolk series is reached in June, 1911, when, on the thirteenth, we have three deaths; on the fifteenth, four; on the twenty-second, four; on the other days ranging from one to three. In this series we have a humidity ranging from 61 to 83, and in addition to this we have the most remarkable spell of heat known for years, running a steady upward course from 67 to 96, but marked at the pinnacles mentioned by exacerbation running as high as 96 and 97.

I have attempted no conclusion, but give out these statistics and facts merely for what they are worth, believing, however, that in a more extensive research there will be found a definite relation of humidity. The appended charts will prove of interest.

Taylor Building.

THE HYPODERMIC USE OF HEMATINICS IN THE TREATMENT OF ANEMIA IN CHILDREN, WITH REPORT OF CASES *

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PHILADELPHIA

The hypodermic use of medicaments calculated to make a deep and rapid impression on the blood and the blood-making organs and to combat certain infections is not new. For many years, in the treatment of secondary and tertiary syphilis, it has been the custom, originally amongst the Latins, and more latterly amongst American clinicians, to administer mercury subcutaneously. For rapidity of effect this method of giving the drug is without a peer. Of late years considerable interest has been directed toward the administration in this manner of drugs whose purpose was to overcome diseases essential to the blood itself, blood dyscrasias and blood deterioration dependent on systemic or local infection or toxemia. The old adage "remove the cause" as the primary act to be accomplished has, with reference to the treatment of many diseases, become stale and trite, and, in a vast number of instances, is more easily said than done. It becomes necessary, therefore, to combat the results of infection or toxemia by placing in the blood current substances which, if they do not destroy the circulating cause, at least mitigate its influence by supplying pabulum which continuously makes up for that which is being destroyed, thereby improving directly the quality of the blood and indirectly combating the etiologic factor.

In no class of cases do the foregoing conditions obtain with greater emphasis than in the anemias of childhood. Here the causative element, either tangible or not, is often not readily destroyed, or if it be, its by-effects remaining for some period, the indication to be met is to increase the amount of hemoglobin and the number of red cells in the blood. Aside from the administration of good food, fresh air and the improvement of environmental conditions, as is well known, the best results are obtained by the administration of so-called hematinics, of which, up to the present, iron and arsenic furnish the best examples. Both, however, interfere with digestion, and the former is absorbed with great tardiness, the largest portion of that ingested being expelled as the sulphid of iron. The latter causes nausea and diarrhea and may seriously

*Read in the Section on Diseases of Children of the American Medical Association, at its Sixty-Third Annual Session, held at Atlantic City, June, 1912.

interfere with kidney function. Thus, whatever good effect may accrue from the use of these drugs *per orem* is often lost, and at the end of a course of treatment the condition for which they were first administered may be made worse. Even in the absence of disturbing symptoms the amount which enters the circulation is infinitesimally small and the progress of the case toward recovery slow. Therefore, if these agents could be placed in the circulation with great rapidity and in sufficient amount not only to overcome the effects of the toxemia, but in slight excess of this, without disturbing the normal progress of metabolism, much in the way of a rapid upbuilding of hemoglobin and red cells could be anticipated, with a disappearance of the anemia, and, as a logical sequence, with an increase in the individual's resistance.

The results obtained by J. L. Morse,¹ detailed in a paper read before this Section in June, 1909, unquestionably prove this to be so. He employed the citrate of iron alone and noted an increase in hemoglobin. In some of his patients the effect on the erythrocytes was minus. This was not noted in my cases, probably on account of the fact that a combination of hematinics was employed, one of which was an arsenical derivative. E. S. Bullock and L. S. Peters² also record a successful experience with the use of the citrate of iron administered hypodermically in 256 cases of anemia secondary to pulmonary tuberculosis in adults. W. J. Barlow and R. L. Cunningham³ treated twenty-eight patients with anemia secondary to tuberculosis and found that iron alone increased the hemoglobin, while the arsenical preparations influenced more profoundly the red cells. They also noted a marked increase in weight. Some of my cases were in adults, but they are not embraced within this report.

Before detailing my results I wish to record my experiences with this method of treatment in an attempt to define its correct status.

Much depends on the character of the preparation employed and the technic of its administration. Therefore, the selection of the preparation is of vast importance in determining the success or failure of the treatment. Strange as it may seem, citrate of iron, a substance known to consist of a definite chemical formula, possesses physical characteristics which are not always identical in samples of the drug furnished by two different pharmacists. I am not aware that the substance is allotropic, but that there exists a difference between different specimens is confirmed

1. Morse, J. L.: The Treatment of Anemias in Infancy with Citrate of Iron Administered Subcutaneously. Jour. Am. Med. Assn., July 10, 1909.

2. Bullock, E. S., and Peters, L. S.: The Use of Hypodermics of Citrate of Iron in the Secondary Anemias of Tuberculosis. Jour. Am. Med. Assn., Oct. 28, 1911.

3. Barlow, W. Jarvis, and Cunningham, R. L.: Effects of Hypodermic Injection in the Secondary Anemia of Chronic Pulmonary Tuberculosis. Jour. Am. Med. Assn., Oct. 28, 1911, p. 1435.

by the two samples which I have here, and also by the fact that the darker one is decidedly irritating, while the lighter one is free of unpleasant local effects. One specimen was prepared by a Philadelphia druggist of excellent reputation, the other by a Cincinnati chemist of equally good repute. Both of these preparations having been exposed to an equal amount of light while in my possession, the change in the one can hardly be said to be due to this factor. Bullock and Peters, while mentioning the fact that local irritation does occur, state that they did not experience it in any of their own cases and ascribe this to the fact that they employed a preparation imported from Italy. Barlow and Cunningham report induration in all their cases which were treated with iron citrate alone, while sodium cacodylate produced none. In my earlier cases I employed $\frac{3}{4}$ of a grain of citrate of iron, as recommended by Morse, but subsequently found $\frac{3}{10}$ of a grain to be as efficient and without systemic toxic effect. As the majority of the patients in my cases here reported exhibited more or less deficiency in the number of red cells, as well as in the percentage of hemoglobin, I have made use of the following combination, unless for some reason, as kidney disease, I have felt that arsenical preparations were contra-indicated:

R		gm. or c.c.
Ferri citratis	gr. $\frac{3}{10}$ or $\frac{3}{4}$	0.018 or 0.045
Sodii cacodylatis	gr. $\frac{1}{2}$ or	0.03
Sodii glycerophosphatis	gr. $1\frac{1}{2}$	0.09
Aquæ destil (Sterile)	mxx	1.30

This appears to have a more rapid and certainly a broader effect than the citrate alone. It is non-irritating and the subjective tonic effect is quickly experienced, this being especially mentioned by adult patients.

TECHNIC

The technic of administration may make for or mar the success of an individual case. An ordinary hypodermic syringe, preferably all glass, is employed. Of course sterilization of the needle and syringe and antiseptics of the site of injection are to be enforced. An ordinary steel needle may be employed if it be washed out with alcohol immediately after use. A gold needle will not rust at all. Platinum needles, I have found to be too soft; they bend and break readily and are expensive to replace. The injection is to be given deep. The needle is held at right angles to the point of injection; it is then quickly plunged to its full length into the underlying tissues. After experimenting on several portions of the body I find that the postero-lateral inner aspect of the upper portion of the arm furnishes the best and least painful site for the injection. The tissues here are loose and readily adapt themselves to the small amount of fluid placed within them.

If the injection be properly made in the majority of instances there will be no pain and no local reaction. The most that is complained of is a slight stinging sensation as the fluid enters the tissues. This may be momentarily severe if a nerve filament be pierced or pressed on. It rapidly subsides, however. There is left behind no soreness, no induration and no abscess-formation. If, however, the fluid be not placed sufficiently deep or some of it enters between the layers of the skin, the local reaction is severe and manifests itself by great pain, swelling, redness which may extend for some distance and induration, which remains over a long period of time. Not infrequently these areas of induration are preceded by severe ecchymoses. I have never encountered abscess-formation. The only accident which I have encountered was in a very nervous child who, in jerking away after the needle had been inserted in the arm, caused the needle to break off *in situ*. It was removed without difficulty at once under cocain and aside from the momentary embarrassment caused no inconvenience.

Systemically there are no immediate effects, unless a dose too large for the individual be given. Under the latter circumstances the following symptoms, as experienced by myself from a dose of gr. $1\frac{1}{2}$ of citrate of iron self administered, may be noted in children or complained of in adults: From two to three minutes after injection there occurs intense vertigo, a feeling of nausea which may proceed to vomiting, a sensation of faintness and weakness, trembling of the legs and arms, cardiac palpitation, increase in the pulse, which becomes small, and the body is bathed in a cold perspiration. After reclining, all these symptoms pass gradually away within fifteen to twenty minutes. Young infants frequently vomit from a dose which is too large for the individual. Likewise the symptoms just detailed may not occur until after several injections are given, each individual injection being free of symptoms, showing that the action of the iron citrate is cumulative. I have noted these symptoms appear toward the end of a course of treatment when the blood picture was normal or much improved and the patient manifested every sign of good health. I have taken this as a sign to discontinue treatment. If the dose be within the maximum for the individual, and this must be determined in each case, it being quite safe to begin with $\frac{3}{4}$ of a grain, there are no systemic ill effects. The only effects are good. The patient's appetite speedily improves, the color is bettered, languor and apathy are replaced by buoyancy and an eagerness for play, and adults note a sensation of revivification, usually voluntarily expressed. These subjective sensations readily find a substantial basis for their existence in a speedy improvement of the quality of the blood. The hemoglobin is rapidly increased and the red cells as well.

In some cases wherein the hemoglobin was materially increased Morse noted a reduction in the number of red cells. In my own series this occurred in but one instance.

The following cases represent the cases in children occurring in my own practice which I have treated within the past three years. Complete blood counts were made in all cases. My report includes twenty cases in children. Although more were treated, this number was regarded as sufficient to illustrate the value of the treatment.

CASE REPORTS

CASE 1.—Z. H., female, aged 12 years. Chlorosis.

June 23, 1909:

Hemoglobin	63%
Erythrocytes	4,240,000
Leukocytes	7,000
Color index74
Achromocytosis and poikilocytosis, present.	
Polymorphonuclears	68%
Small lymphocytes	24%
Large lymphocytes	6.5%
Eosinophils	1.00
Basophils5

Eight injections.

July 28, 1909:

Hemoglobin	89%
Erythrocytes	4,320,000
Leukocytes	7,200
Color index92
Blood normal in appearance.	

CASE 2.—B. G., female, aged 14 years. Chronic parenchymatous nephritis.

July 3, 1909:

Hemoglobin	55%
Erythrocytes	4,950,000
Leukocytes	10,800
Color index55
Six injections of ferri citratis, gr. 3/5.	

July 12, 1909:

Hemoglobin	60%
Erythrocytes	5,410,000
Leukocytes	9,400
Color index55
Nine injections.	

Nov. 9, 1909:

Hemoglobin	87%
Erythrocytes	4,790,000
Leukocytes	8,400
Color index87

CASE 3.—A. E., female, aged 3 years. Inherited syphilis; general adenopathy.

July 3, 1909:

Hemoglobin	56%
Erythrocytes	3,000,000
Leukocytes	10,000
Color index93
Polymorphonuclears	50%
Small lymphocytes	42%
Large lymphocytes	6%
Eosinophils	2%

Stained specimen shows general achromocytosis, microcytes, macrocytes.

Mercurial inunctions and nine injections.

Sept. 5, 1909:

Hemoglobin	83%
Erythrocytes	4,200,000
Leukocytes	9,800
Color index98

CASE 4.—E. O., female, aged 4 years. Cyclic vomiting; acetoneuria.

Aug. 3, 1909:

Hemoglobin	62%
Erythrocytes	240,000
Leukocytes	8,200
Color index	1.29
Polymorphonuclears	72%
Small lymphocytes	20%
Large lymphocytes	9%

Six injections.

Sept. 7, 1909:

Hemoglobin	78%
Erythrocytes	3,230,000
Leukocytes	8,500
Color index	1.20

Seven injections.

Oct. 3, 1909:

Hemoglobin	87%
Erythrocytes	4,190,000
Color index	1.03

CASE 5.—E. R., female, aged 14 years. Rapid growth in past six months. Menstruated once. Languor, anorexia, pica.

Oct. 25, 1909:

Hemoglobin	64%
Erythrocytes	3,921,000
Leukocytes	6,800
Color index81
Polymorphonuclears	53.7%
Small lymphocytes	28.8%
Large lymphocytes	13%
Eosinophils	4.44%
Basophils06%

Erythrocytes have pale centers, few macrocytes, numerous microcytes, occasional poikilocytes.

Six injections.

Nov. 4, 1909:

Hemoglobin	81%
Erythrocytes	4,410,000
Leukocytes	8,900
Color index91
Polymorphonuclears	66%
Small lymphocytes	26%
Large lymphocytes	7%
Eosinophils	1%

Red cells still visibly deficient.

Seven injections.

Nov. 28, 1909:

Hemoglobin	88%
Erythrocytes	5,290,000
Leukocytes	7,800
Color index84

Red cells normal in every respect.

Total number of injections 13.

CASE 6.—K. McD., female, age 12. Very studious, choreic, constipated, anorexia, indicanuria.

Nov. 4, 1909:

Hemoglobin	70%
Erythrocytes	4,240,000
Leukocytes	68,000
Color index84

Achiomocytosis general, many microcytes, few poikilocytes.

Polymorphonuclears	51%
Small lymphocytes	13%
Large lymphocytes	28%
Eosinophils	6%
Basophils	2%

Eight injections.

Nov. 31, 1909:

Hemoglobin	82%
Erythrocytes	4,800,000
Leukocytes	7,200
Color index85

Achromocytosis present, but less marked. Microcytes less, few poikilocytes.

CASE 7.—A. D., female, aged 10. Just recovered from post-scarlatinal nephritis.

Nov. 12, 1909:

Hemoglobin	69%
Erythrocytes	3,982,000
Leukocytes	7,800
Color index87

Decided achromocytosis.

Polymorphonuclears	53%
Small lymphocytes	33.6%
Large lymphocytes	13.0%
Eosinophils2%
Basophils2%

Nine injections.

Dec. 18, 1909:

Hemoglobin	86%
Erythrocytes	4,310,000
Leukocytes	7,600
Color index99

General appearance of blood quite normal.

CASE 8.—I. B., male, aged 4 weeks. Sepsis neonatorum, wasted; metastatic abscess.

April 28, 1910:

Hemoglobin	30%
Erythrocytes	1,330,000
Leukocytes	13,000
Color index	1.12

Five injections.

May 6, 1910:

Hemoglobin	38%
Erythrocytes	1,600,000
Leukocytes	14,000
Color index	1.18

Died of general sepsis.

CASE 9.—B. L., female, aged 13. Rheumatic purpura.

Aug. 5, 1910:

Hemoglobin	60%
Erythrocytes	4,100,000
Leukocytes	14,000
Color index73

Achromocytosis, microcytes and poikilocytes present.

Polymorphonuclears	65%
Small lymphocytes	24%
Large lymphocytes	8%
Eosinophils	3%

Fourteen injections.

Sept. 6, 1910:

Hemoglobin	90%
Erythrocytes	4,500,000
Leukocytes	12,000
Color index88

CASE 10.—A. H., male, aged 6 years. Cyclic vomiting.

Aug. 31, 1910:

Hemoglobin	60%
Erythrocytes	3,600,000
Leukocytes	16,000
Color index83
Polymorphonuclears	68%
Small lymphocytes	23%
Large lymphocytes	7%
Eosinophils	2%

Seven injections.

Oct. 2, 1910:

Hemoglobin	83%
Erythrocytes	4,200,000
Leukocytes	11,000
Color index98

CASE 11.—A. S., female, aged 13 years. Acute articular rheumatism; rheumatic endocarditis of mitral valve.

Sept. 22, 1910:

Hemoglobin	40%
Erythrocytes	3,800,000
Leukocytes	7,600
Color index52
Polymorphonuclears	68%
Small lymphocytes	22%
Large lymphocytes	8%
Eosinophils	2%

Red cells quite uniformly deficient in hemoglobin.

A few microcytes and poikilocytes present.

Nine injections.

Nov. 18, 1910:

Hemoglobin	85%
Erythrocytes	4,300,000
Color index9

General appearance normal.

CASE 12.—A. H., male, aged 3 years. General adenopathy and objective pallor.

Oct. 13, 1910:

Hemoglobin	58%
Erythrocytes	2,900,000
Leukocytes	14,000
Color index	1.00
Polymorphonuclears	62%
Small lymphocytes	26%
Large lymphocytes	11%
Eosinophils	1%

Microcytes, macrocytes, poikilocytes present; eight injections.

Nov. 9, 1910:

Hemoglobin	80%
Erythrocytes	4,200,000
Leukocytes	11,600
Color index92
Polymorphonuclears	65%
Small lymphocytes	28%
Large lymphocytes	5%
Eosinophils	2%

Jan. 15, 1911: Just recovering from an attack of double otitis media and acute non-suppurative cervical adenitis.

Hemoglobin	48%
Erythrocytes	3,600,000
Leukocytes	6,200
Color index66

Seven injections.

Feb. 18, 1912:

Hemoglobin	82%
Erythrocytes	4,300,000
Leukocytes	6,300
Color index93

CASE 13.—B. H., female, aged 9 years. Nervous, anorexia.

Jan. 15, 1911:

Hemoglobin	72%
Erythrocytes	2,810,000
Leukocytes	9,000
Color index	1.28

March 5, 1911:

Hemoglobin	78%
Erythrocytes	2,900,000
Leukocytes	8,400
Color index	1.39

Total number of injections three. Discontinued treatment on account of nervousness.

CASE 14.—Baby P., male, aged 9 weeks. Malnutrition; gastro-intestinal catarrh; pertussis.

Feb. 9, 1911:

Hemoglobin	31%
Erythrocytes	2,600,000
Leukocytes	4,600
Color index69

Achromocytosis, microcytes, poikilocytes present.

Twelve injections.

March 5, 1911:

Hemoglobin	49%
Erythrocytes	3,100,000
Leukocytes	7,200
Color index79

Achromocytosis, microcytes and poikilocytes present.

General condition much improved.

CASE 15 —E. G., female, aged 13 years. Chlorosis.

Feb. 15, 1911:

Hemoglobin	64%
Erythrocytes	4,140,000
Leukocytes	8,400
Color index74

Achromocytosis marked.

Polymorphonuclears

Small lymphocytes

Large lymphocytes

Eosinophils

Seven injections.

March 18, 1911:

Hemoglobin	85%
Erythrocytes	4,300,000
Leukocytes	8,500
Color index98

Red cells appear healthy.

CASE 16.—Baby C., aged 10 months. Malnutrition; scurvy.

April 8, 1911:

Hemoglobin	40%
Erythrocytes	3,100,000
Leukocytes	8,000
Color index64
Polymorphonuclears	68%
Small lymphocytes	22%
Large lymphocytes	10%
Six injections.	

April 27, 1911:

Hemoglobin	65%
Erythrocytes	4,000,000
Leukocytes	8,200
Color index81
Six injections.	

May 10, 1911:

Hemoglobin	80%
Erythrocytes	4,250,000
Leukocytes	9,800
Color index94
Total number of injections twelve.	

CASE 17.—S. L., female, aged 12 years. Furunculosis; chlorosis.

Jan. 17, 1911:

Hemoglobin	69%
Erythrocytes	3,000,000
Leukocytes	14,000
Color index88
Achromocytosis.	
Polymorphonuclears	74%
Small lymphocytes	18%
Large lymphocytes	7%
Eosinophils	1%
Treated with stock vaccines, Brewer's yeast, followed by six injections.	

March 5, 1911:

Hemoglobin	76%
Erythrocytes	4,100,000
Leukocytes	12,000
Color index90
Same treatment. Six injections.	

April 9, 1911:

Hemoglobin	85%
Erythrocytes	4,420,000
Leukocytes	10,000
Color index96

CASE 18.—M. B., female, aged 9 years. Chorea, rheumatic endocarditis of mitral valve.

Aug. 16, 1911:

Hemoglobin	68%
Erythrocytes	3,800,000
Leukocytes	12,600
Color index9
Polymorphonuclears	68%
Small lymphocytes	23%
Large lymphocytes	8%
Eosinophils	1%
Complete recovery after three months' rest in bed.	
Nine injections after acute symptoms subsided.	

Dec. 1, 1911:

Hemoglobin	85%
Erythrocytes	4,200,000
Leukocytes	8,000
Color index	1+

CASE 19.—J. H., female, aged 6 years. Chronic gastro-intestinal indigestion, night terrors, lithuria, indicanuria, chlorotic type of blood.

Jan. 21, 1912:

Hemoglobin	71%
Erythrocytes	4,100,000
Leukocytes	6,200
Color index86
Polymorphonuclears	62%
Small lymphocytes	27%
Large lymphocytes	11%

Treated 1 month, eight injections.

April 27, 1912: After attack of varicella.

Hemoglobin	82%
Erythrocytes	4,100,000
Leukocytes	7,200
Color index	1.00

CASE 20.—S. S., male, aged 5 years.

March 20, 1912:

Hemoglobin	60%
Erythrocytes	3,500,000
Leukocytes	7,300
Color index88
Polymorphonuclears	63%
Small lymphocytes	23%
Large lymphocytes	13%
Eosinophils	1%

Fourteen injections.

April 25, 1912:

Hemoglobin	85%
Erythrocytes	4,200,000
Leukocytes	7,900
Color index	1+

In all, 202 injections were given. All patients, save Case 19, received the combination of hematinics originally stated. In Case 19, because of the kidney lesion, the patient received ferri citratis gr. $\frac{3}{4}$ alone. The average number of injections to a case was a little over ten. The highest number of injections given in a single case was fifteen. In Case 13 the patient received the lowest number, three injections. All of the patients were rapidly benefited by treatment, except in Cases 8, 13 and 14. In Case 8 the condition was hopeless from the beginning, the infant, 4 weeks old, succumbing to general sepsis and metastatic abscesses. Even in this patient, however, the five injections given raised the hemoglobin from 30 per cent. to 38 per cent. in one week. The patient in Case 13 reported irregularly for treatment, and while showing a very slight increase in hemoglobin and red cells, remained practically unchanged. In Case 14 the patient received regular and continuous treatment, but showed very little improvement. The infant throughout the course suffered from chronic gastro-intestinal indigestion and nearly died of pertussis and

bronchopneumonia. At the age of over two years the mother writes me from New York that its physical condition is very good.

In Case 12 the patient received fifteen injections over a period of four months and illustrates well the tonic effect of the treatment. In a little less than one month after eight injections his hemoglobin rose from 58 per cent. to 80 per cent., and his red cells from 2,900,000 to 4,300,000. A severe attack of non-suppurating, but lingering bilateral cervical adenitis and double otitis media reduced this again to 48 per cent. hemoglobin and 3,600,000 red cells. Seven injections in a little over four weeks brought them up again, respectively, to 82 per cent. and 4,300,000.

CONCLUSIONS

1. In the hypodermic injection of hematinics we possess a quick, safe and reliable means of treating the anemias of childhood.
2. A combination of iron and arsenic compounds seems to have a better effect than either alone.
3. Small doses of each give as good results as large ones.
4. The tonic effect is noted almost immediately after beginning treatment.
5. The injections should be made deep in loose tissue.

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PELLAGRA IN CHILDREN *

(A PRELIMINARY REPORT)

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Pellagra has existed for any length of time on the North American continent only in Mexico. Since 1864, cases of the disease have from time to time been reported in the United States. Except for a few sporadic cases, however, it is doubtful if pellagra was existent in this country prior to the year 1900. In the fall of 1906, an increasing number of puzzling cases developed at the Mount Vernon (Ala.) Asylum for insane negroes. A few such cases had been observed in the institution since the summer of 1901, but were diagnosed no more definitely than cases of "marked general debility." The rapid spread of the malady aroused the institutional authorities to a more zealous study of the disease for the purpose of control.

Dr. G. H. Searcy, assisted by Dr. Isadore Dyer, New Orleans, and Drs. McCafferty and Somerville, Mt. Vernon, worked out these cases, eighty-eight in all, and reported them as pellagra at the meeting of the State Medical Association of Alabama, April 19, 1907. Important and significant facts brought out in this study were as follows:

1. More than 90 per cent. of the cases were in females.
2. No nurse contracted the disease. The nurses' association with the inmates were very close, handling them frequently and sleeping in halls adjoining and opening into their rooms; living, altogether, very much the same life except in regard to diet.
3. The main article of diet with the inmates was corn bread. The nurses ate biscuits and light bread and had a more varied diet. A sample of the meal used was examined by a government expert and was found to be moldy, full of fungi and bacteria.
4. The spread of the disease was immediately checked when the corn bread diet was changed. For test purposes eight inmates, apparently free from symptoms at the beginning of the test, were kept on bread made from the meal examined. One of these very shortly developed pellagra, another began to show symptoms, and all displayed so rapid a decline in health that the experiment was discontinued.

*Read in the section on Diseases of Children of the American Medical Association at the Sixty-Third Annual Session, Atlantic City, June, 1912.

These findings are given in some detail for two reasons: (1) Searcy's report, which contained a warning to physicians in the south to be on the lookout for the disease, did not attract the attention it so richly deserved; (2) the findings conform closely to observations made by many previous writers in Europe and by later writers in the United States.

In the same year, 1907, but working independently, Dr. J. W. Babcock reported the existence of pellagra among the inmates of the State Insane Asylum at Columbia, S. C.

Babcock has made some excellent studies on the disease. He deserves especial credit for creating a widespread interest in pellagra and for provoking others to give to the subject serious thought and study.

The United States Public Health and Marine-Hospital Service early had men in the field making extensive and intensive studies. The men in this service have done much to promote educational work on pellagra. They are liberal contributors to the symposia on the subject, without which for several years past no medical meeting in the southern states has been regarded as complete.

The disease is now readily recognized and is promptly reported whenever it makes its appearance in a new community.

Medical journals are devoting much space to the discussions on pellagra; the Public Health and Marine-Hospital Service has issued some valuable bulletins and publications; several text-books by American authors have been placed on the market; the literature on the disease in this country is becoming voluminous.

A review of the literature, carefully selected but comprehensive, reveals the following to be some of the more important findings relative to pellagra as it exists in the United States:

1. The disease is spreading with startling rapidity.
2. More females than males contract the disease.
3. The disease is not contagious.
4. No age is exempt, but young adults between 30 and 40 years seem to be slightly more susceptible.
5. Pellagra attacks both whites and blacks and in about the same proportion. Jews apparently enjoy immunity.
6. Occupations requiring indoor life seem to favor its development.
7. Pellagra occurs more frequently in the rural population than in the population of cities. On the other hand, it is met with more commonly in penitentiaries, insane asylums, orphan asylums, mining camps, cotton mills and factory villages, etc., than in the country.
8. Pellagra, as a rule, is found amidst insanitary conditions. It occurs, too, in homes which in themselves are of good sanitary and

economic condition, but which adjoin some mining camp or mill village in which the disease exists. Again, breaking all rules, it attacks, not infrequently, the well-to-do city dweller, living under modern hygienic conditions.

9. Any ailment causing a run-down condition predisposes to pellagra. The disease is so commonly met with in persons infected with hookworm or ameba that some investigators have convinced themselves of a direct causal relation between pellagra and these intestinal parasites. Pellagra frequently develops after pregnancy, prolonged lactation, tuberculosis, typhoid fever, etc. Alcoholics are more susceptible than persons of temperate habits.

10. Pellagra favors the warmer climates of the southern states.¹ It is much influenced by season. New outbreaks invariably occur in the spring or summer months. Symptoms in pellagrins are much relieved and often disappear in cold weather, only to reappear the following spring. Symptoms, especially of the skin, are aggravated by exposure to the sun's rays.

11. The cause of pellagra is still unknown. It has been observed that pellagra made its appearance in the south, where cornmeal has been a popular article of diet for many years, about the time the corn crops in this section of the country became insufficient to supply the demand, and when shipped meal of an inferior quality came into general use.

That pellagra is in some way connected with the use of corn as an article of diet is an opinion almost as old as the disease itself. The entrenchment of this idea in the minds of a majority of those connected with the study of pellagra has been repeatedly and often brilliantly assailed. In support of Sambon's theory that pellagra is a parasitic disease transmitted by the buffalo gnat, it has been observed that in this country, too, many houses and villages in which pellagra exists are situated near to running streams or branches, in some of which, at least, the larva of *Simulium* has been looked for and found; and that in its behavior the disease suggests itself as being one of place and locality.

The idea, however, that pellagra is a food-poisoning, in some way connected with the use of corn as an article of diet, is still the dominant one. This fact alone does not make that idea right. While theories continue to multiply, opportunity yet remains for some medical worker in the United States to demonstrate the real cause of the disease.

1. Swan, *Southern Med. Jour.*, July, 1911, has pointed out the fact that there are probably many cities and localities outside the lower austral zone which have a sufficient maximum temperature for a part of the year, and a sufficient total heat to fulfill the requirements essential for the development of the so-called tropical and semi-tropical diseases.

12. The last finding of this review was that data relating to pellagra in children is, in this country, very meager. With but few exceptions no case reports of this disease in children have been published. The few cases in print have been brought out to illustrate some phase, other than the possible modifications of the disease in children.

Aside from the mere mention of the fact that young infants and children may be attacked, scant attention has been given to the pellagra of childhood.

It was this finding that prompted me to undertake the paper in hand, not so much with the expectation of adding to the literature anything which in itself would be regarded as valuable, but with the hope of suggesting a profitable line for fuller investigation.

The data in the study to follow was accumulated from three of my own cases, from personal interviews and from replies to letters addressed by me to sixty physicians, who for the most part have had wide experience with pellagra. The questions contained in the letter were as follows:

1. Age of youngest child in which you have observed undoubted pellagra?
2. Age of youngest child in which you suspected, but were unable to positively diagnose, pellagra?
3. What proportion of your pellagra cases have been children under fifteen years of age?
4. What differences, if any, have you noted in the symptoms of pellagra in children and in adults?
5. What difference, if any, in the mortality?
6. Do you regard heredity as an etiologic factor? Why?
7. Have you any evidence that the disease can be carried from mother to child through the agency of the mother's milk? Any contra-evidence?

Forty-eight replies were received. Fifteen, however, replied that they had not encountered pellagra in children. Two of the fifteen were superintendents of institutions in which the inmates were all adults. Five out of eight pediatric men who were written to, had not met with the disease in children; of the remaining number who had not encountered the disease in children, seven live in good-sized towns or cities. Only one lives in a small country town. The combined cases seen by eight pediatric men, all living in cities, number only six. Five of these cases, to my knowledge, were referred from either the country or a village to the city for treatment. These facts very strongly suggest that city children enjoy immunity to a considerable degree.

The answers to Question 1 regarding the youngest age at which undoubted pellagra was observed were as follows:

2 months, age given by 1 correspondent.
4 months, age given by 1 correspondent.
5 months, age given by 1 correspondent.
6 months, age given by 2 correspondents.
15 months, age given by 1 correspondent.
18 months, age given by 1 correspondent.
2 years, age given by 7 correspondents.
3 years, age given by 5 correspondents.
4 years, age given by 2 correspondents.
5 years, age given by 3 correspondents.
6 years, age given by 2 correspondents.
7 years, age given by 1 correspondent.
8 years, age given by 1 correspondent.
10 years, age given by 1 correspondent.
13 years, age given by 1 correspondent.
14 years, age given by 1 correspondent.

Two correspondents reported having met with the disease in children, but had kept no record of their ages.

It is seen that while pellagra may occur in the very youngest infant, it is met with much more frequently after the eighteenth month.

In reply to Question 2, as to the age of the youngest suspected case, twenty answered that no unconfirmed cases of the disease in children had been seen by them. Six either did not answer or answered in such a way as to indicate that the question was not understood. Five answered as follows:

1. Youngest suspect, 9 months. Gave age of youngest undoubted case, 2 years.
2. Youngest suspect, 12 months. Gave age of youngest undoubted case, 3 years.
3. Youngest suspect, 18 months. Gave age of youngest undoubted case, 3 years.
4. Youngest suspect, 2 years. Gave age of youngest undoubted case, 4 years.
5. Youngest suspect, 9 years. Gave age of youngest undoubted case, 3 years.

The question was put for the purpose of eliciting information as to whether in young infants and children, modifications of symptoms sufficient to prevent ready recognition occurred with such frequency as to demand consideration.

Personal experience is at variance with the twenty who answered that no unconfirmed cases had been observed. I have seen one girl 20 months old, and another girl 11 years old, in both of whom I strongly suspected pellagra, and in neither of whom was I able, after exhausting all procedures of elimination known to me, to fix the diagnosis on pellagra or on anything else.

This experience induces me to attach more weight to the answers of the five, who have had suspected cases, than their number may justify. The personalities back of the five answers, however, add weight. Each represents an individual of prominence in the medical world. Some significance, to my mind, attaches itself to the fact that four out of the five suspected patients were younger than the youngest undoubted pellagra patient observed by the respective correspondent. Time for further investigation on this phase of the study is desired.

To Question 3, as to the proportion of children among their pellagra cases, twenty-two answered definitely. The lowest was 1 per cent., the highest was 50 per cent. The average for the twenty-two being 10.5 per cent. A conservative estimate would be that about 10 per cent. of all pellagrins are children under 15 years of age.

To Question 4, regarding symptoms, only three out of thirty-three failed to reply. Thirteen had noted no symptoms in children differing from the symptoms in adults. Seventeen had noted more or less differences. Fifteen of the seventeen agreed that the nervous symptoms in children were less marked than in adults. Three limited the differences between the child type and the adult type of the disease to the nervous symptoms. Five said the disease ran a more acute course in children, but with generally milder symptoms. One of this group of five said that the intestinal symptoms in young children were sometimes more troublesome than in adults. Seven emphasized the fact that the symptoms in children were "very much more mild." One said the symptoms in children were worse than in adults. One said the symptoms were classical in children except for a special tendency to intestinal derangement of severe nature.

Between the group embracing those who observed no differences in symptoms and those who regarded the symptoms as worse in children on the one hand, and the group embracing all those who saw more or less marked differences in favor of children, on the other hand, it is to be regretted that a comparative study cannot be made from the standpoint of the number of cases observed by respective groups. When given the proportion of pellagrous children observed was considerably less with the former than with the latter group. With the pictures of three cases personally studied and the letters received from a number of able workers before me, I am convinced that marked nervous symptoms in pellagrous children are not commonly met with; that frequently the nervous symptoms are not in evidence at all in such cases; that as a general thing the symptoms of pellagra in children, with the possible exception of the eruption, are not so well marked as in the adult; and that not uncommonly, the eruption may be the only symptom prominently manifest.

From a letter recently received from Dr. E. M. Mason, Birmingham, Ala., who has seen an unusual number of both adult and juvenile pellagrins, the following is quoted:

I have seen probably twenty cases of pellagra in children under 12 years of age. In all the cases, the skin symptoms were prominent, and more so than other signs. All the children were well nourished, seemed not to feel badly, and complained very little. Diarrhea and nervous symptoms were not pronounced.

The above description fits the three cases observed by me. These children played and seemed to enjoy life as fully as any normal child.

One of the three was a negro boy 5 years old, who was seen in the second summer of his attack. His body was fairly well nourished, his appetite was good, he slept well, did not complain of pain, but did, at times, complain of being tired and would not play like other children. His mind was bright and no nervous symptoms at all were in evidence. The eruption on hands, neck and feet was typical.

The other two cases were little girls. One was seen in the fall after the eruption had persisted all summer; the other was seen for the first time by me three weeks prior to this report, just ten days after the eruption appeared. Except for a sore mouth in the first girl and for their eruptions, both apparently enjoyed good health.

In answer to Question 5, nineteen regarded the mortality in children as less than in adults, ten of the nineteen answering "much less in children." Seven regarded the mortality as being about the same. One said it was higher in children. Six did not answer.

To Question 6, regarding heredity, all answers but six were negative. These six expressed the opinion that heredity should be considered, but only in so far as a weakened constitution inherited from pellagrous parentage might predispose to the disease.

Unfortunately Question 7 was not added to the letter form until the study had progressed for some time. Only eleven replies containing data on this point were received. Nine had seen pellagrous mothers, who had been or were nursing infants without any evidence of the disease being manifest in the latter. Although the number of infants so observed was not given in all of the nine answers, at least thirteen babies are here represented.

The youngest pellagrin reported to me, 2 months old, nursed a pellagrous mother for four weeks. The baby was then fed on malted milk. The mother died of pellagra when the infant was six weeks old. "The erythematous rash did not appear until several days after the mother's death, but I was informed by the midwife who attended the mother that the infant was much emaciated at birth and had been affected with a profuse, foul-smelling diarrhea since one week old.²

The above case presents several interesting problems. Was pellagra contracted in utero? Was it transmitted through the mother's milk? or was it contracted in neither way, but through some other agency? While these questions are worthy of consideration, until further data is forthcoming, speculations would add length but not depth to the study in hand.

Another reported three infants dying while nursing pellagrous mothers. He did not know whether these infants had pellagra or not. He attended none of them, but he was reliably informed that all three had bowel disorders.

2. Letter received from Dr. T. C. Savage, Jefferson, Alabama.

I regret that I have not sufficient data in hand to justify my position in insisting that the infant should not be permitted to nurse the pellagrous mother. Certainly the possibility of transmitting the disease in this way has not been disproved. On the other hand, can the pellagrous mother or any mother whose constitution is overwhelmed with disease, give a milk suitable for the nourishment and the development of her infant? It ought to be readily admitted that the tax on her system incident to lactation would unfavorably influence the prognosis of the pellagrous mother's own case.

In closing I would respectfully request all those in possession of any data that might throw light on the points brought out in this paper to kindly submit them to me for a future and a more elaborate report.

Woodward Building.

PROGRESS IN PEDIATRICS

THE WASSERMANN-NEISSER-BRUCK REACTION *

PROF. DR. A. JESIONEK
GIESSEN

ABSTRACTED BY HARVEY PARKER TOWLE, M.D.
BOSTON

Jesionek has published a critical review of the literature on the subject of the Wassermann reaction in syphilis which is unusually complete in extent and judicious in tone. The discovery of the *Treponema pallida* was followed so soon by the publication of Wassermann's serologic method of diagnosis and the latter so quickly by Ehrlich's method of chemotherapy that the intervals were too short to allow the study of any to be completed before the interest of the medical public was attracted to its successor. This diversion of attention has particularly followed Ehrlich's discovery. The interest which it has excited would seem almost to have produced forgetfulness of the fact that many phenomena concerning the *Treponema pallida* and the Wassermann reaction still await explanation. Therefore, Jesionek's article may help us to regain some of our lost perspective with regard to the Wassermann method of serodiagnosis.

The articles on the subject are arranged, for the purpose of this critical review, into two groups. In the first are placed those papers which have to do with the chemistry and the technic of the reaction. This group need not be considered here as it has been so recently reviewed in this journal by Lucas.¹ We may, therefore, confine our attention to the second division which deals with the literature on the clinical relationship of the reaction to syphilitic disease.

Jesionek concludes from his study that it may be accepted without further comment that the Wassermann reaction gives a positive guide in the presence of *active* cutaneous manifestations of disease; when positive, always declaring them to be syphilis. When, however, the intermediate cases are encountered, in which the cutaneous manifestations are dubious or lacking, it would seem that even the positive Wassermann reaction is not entirely convincing.

In order to demonstrate the value of the reaction and its interpretation, Jesionek has subdivided the articles of the second group. First, he takes up those on the question of the clinical specific nature of the reaction. His conclusion, given in his own words, is that the original idea of a clinical specificity of the reaction for syphilis cannot be

*Jesionek, A.: *Praktische Ergebnisse auf dem Gebiete der Haut- und Geschlechtskrankheiten*, 1, 286, 1912.

1. Lucas, W. P.: *The Wassermann Reaction in Syphilis: A Résumé of Current Literature*, *AM. JOUR. DIS. CHILD.*, 1912, iii, 259.

sustained from either a biologic or a clinical point of view. As a matter of fact, there is a large number of diseases, besides syphilis, in which one can, now and then, obtain a positive reaction. First of all in this connection, Jesionek mentions *frambesia tropica*, lepra, scarlet fever and the trypanosome diseases. Of chief interest to the pediatricist, however, is the statement that *scarlet fever* gives a *positive reaction* in approximately 40 per cent. of the cases. Naturally, the need of a differential diagnosis between syphilis and scarlet fever is a rarity.

In commenting on the occurrence of the positive reaction in these non-syphilitic affections, it is stated that one causative factor may be the difficulty of the technic. This factor would apply equally well to every reported reaction, as the method demands that none but the most highly trained specialists shall attempt it. His comment is, therefore, that, before accepting the apparent results of the test, we should examine into the conditions under which the test is made. Nevertheless, there is no question, even on these grounds, but what the test reacts positively in certain non-syphilitic diseases as is manifested by the reports of a number of especially well qualified investigators. According to Weil and Braun, in all these non-syphilitic cases with positive reactions the one common factor present is a morbid alteration of the organs, cell changes and resorption of cell products. These exceptions do not injure the practical meaning of the reaction, but merely call attention to the need of care in estimating the significance of individual factors. Jesionek quotes Lesser as saying:

There is never a positive reaction except in the presence of syphilis or a justified suspicion of syphilis—to which we wish to add the words *Cave Scharlach*.

As a matter of practice one would do well, in the presence of a positive reaction, to think first of syphilis, at the same time remembering that occasionally, although seldom, there occur in connection with other diseases such alterations in the blood serum as find their visible expression in the positive result of the reaction of complement-fixation.

According to the investigations of Seligman and Blume, it seems as if such affections as tumors, phthisis and sepsis, which cause "a powerful consumption," have a tendency to form substances which may give a positive reaction with one or another extract. Furthermore, it is noticeable that the reaction is very frequently positive in sera obtained after death.

In regard to the relationship of the reaction to syphilis as revealed by the literature, Jesionek asks: "Do all syphilitics give a positive reaction?" "If not, why does the reaction behave differently in one case of syphilis than in another? What conclusions are to be drawn from the variable results of the reaction in the individual syphilitics?" He then gives the general answer that a positive reaction is present in nearly every case in which the symptoms are florid. That is to say, not every case

which we may consider syphilitic on the ground of its history or clinical symptoms gives a positive reaction. In general, it can be said that the statistics at hand establish the fact that a positive reaction is obtained in only about 50 per cent. of the total cases of acknowledged syphilis. From this fact is drawn the fundamental conclusion that the negative reaction has no value in the differential diagnosis of syphilis or non-syphilis. Under no condition does a single negative reaction justify the conclusion that syphilis does not exist.

Next, in order to make clearer the meaning of the positive reaction and its relation to the syphilitic disease process, Jesionek reviews the subject from the standpoint of the different disease periods. Without going into details, it may be said that, in the primary stage, the reaction does not become positive, as a rule, until after eight or ten weeks, whereas, in the early secondary stage, it is positive almost without exception. The reason given for this difference is that in the first, the early, period of the primary stage, the disease has not yet become a true systemic infection. On the other hand, in and just preceding the secondary period the infectious processes are at their height and the spirochetes have invaded the whole organism.

As already noted, the reaction is occasionally negative even when the symptoms are "florid." In the light of the statement that "before accepting a result we must investigate the manner of its making," the following comments are especially worthy of note:

We cannot at present definitely explain why such cases (the florid) should give a negative reaction. One point, however, should be emphasized, i. e., that more than one blood examination is necessary to firmly establish the negativity of a manifest syphilis. It frequently happens that the positive result of the second examination throws doubt on the negative finding of the first. The great technical difficulties and the numerous sources of error which complicate every examination throw suspicion on every unusual behavior.

Nearly all investigators obtain a smaller percentage of positive results in tertiary syphilids than in secondary. For example, Brück reports positive results in about 90 per cent. of the secondary syphilids, but only 70 to 80 per cent. in the tertiary. Blascho emphasizes the fact that a negative reaction was strikingly frequent in bone affections, even in out-spoken, painful gummata and in undoubted syphilitic bony exostoses. He has also repeatedly found the reaction negative in syphilitic disease of the kidneys. Jesionek believes that the reaction is negative in gummata of the brain quite as frequently as it is in disease of the bones, "which is all the more curious as the parasymphilitic affections of the brain give rise to a positive reaction quite regularly."

On the other hand, as regards the negative reaction, the difficulty of diagnosing tertiary syphilis of the viscera must not be overlooked. One forgets, only too easily, that a "syphilitic" individual can now and then be ill in other than a specific manner.

All in all, however, one may conclude that tertiary syphilis in patients with undoubted syphilitic symptoms yields positive results as frequently as in patients with secondary manifestations. From this fact Jesionek concludes that in the presence of doubtful symptoms the diagnosis must be syphilis if the reaction is positive.

In congenital syphilis the same laws apply as in acquired syphilis. Therefore, it is no surprise to find that the blood of congenital syphilitics, at least so long as they show manifest symptoms, practically always gives a positive reaction. The Wassermann reaction confirms the clinical observation that syphilitic parents may bear children who never show a trace of syphilitic disease. Such children, however, always give a negative reaction to repeated tests. On the other hand, it happens not infrequently that the reaction is positive in children in whom no clinical symptoms have developed, the sole manifestation of their disease, therefore, lying in the alteration in the blood, which is demonstrated by the complement fixation reaction.

The mothers of syphilitic children react positively practically without exception, notwithstanding the fact that they may show no specific, organic changes. As concerns the relationship of the Wassermann reaction to the laws of inheritance, it can be said that immunity does not exist in the sense of the Baumes-Colles law, but that the so-called immune mothers of syphilitic children as a rule react positively. This means that the mothers carry within themselves an active syphilitic poison and are, therefore, subject to the same conditions as other syphilitic individuals.

LATENT SYPHILIS

In any consideration of the relationship of the Wassermann reaction to syphilis its behavior in the so-called "latent periods" must not be overlooked. According to Jesionek, the reaction is present in fewer cases when the disease is "latent" than when active, but is present oftener in the early latent period than in the late. It is a fact of common agreement that there has been discovered no law which governs the appearance of the positive reaction in the late periods of latency. It seems to occur as frequently thirty to forty years after infection as after only five or ten years. Jesionek suggests that latent syphilitics possess a high antibody content and contends that the positive reactions denote the existence of active syphilis in the patients.

Jesionek next discusses the meaning of the term "latency." In his opinion, so long as the case manifests even the slightest trace of disease, the term latent is inappropriate. Therefore, pigmentation from a pre-existing macule or papule, enlarged glands, disturbances of sensation and the like, remove the case in which they occur from the "latent" class. There are cases, however, in which the disease is actually latent. At the

end of the first year and in the second and third years of the disease there may remain not the slightest discoverable trace of the syphilitic infection. Neither glandular infections nor suspicious pigment anomalies exist. The patient enjoys the best of objective and subjective well-being. But, Jesionek continues, it is characteristic of the syphilitic virus to apparently slumber for years and tens of years, only to suddenly wake into activity. The reason we do not know. Possibly, conditions exist in the host which prevent the spirochetes from exercising their pathogenic properties. We know, for example, through histologic research, that in congenital syphilis the organism may be overrun with spirochetes and nevertheless manifest no changes which can be regarded as specific.

Regarding the occurrence of a positive reaction in the late period of latency, Jesionek believes that chance cannot account for the fact that the percentage of cases which, escaping diagnosis during life, are discovered at autopsy to be syphilitic agree so closely with the percentage of cases giving a positive Wassermann reaction in life, notwithstanding the complete absence of clinical symptoms.

Unfortunately, the Wassermann reaction cannot distinguish between cure and latency. In both conditions there is the same lack of symptoms. The Wassermann reaction, however, does not tell us in which case the infectious agent has been destroyed and in which it is liable to burst into activity again. As a rule, the reaction changes from negative to positive as soon as clinical symptoms reappear. Occasionally, however, the change occurs without accompanying clinical signs.

WASSERMANN REACTION AS A SYMPTOM

With this, we come to the weightiest point in the whole subject of the relation of the Wassermann reaction to syphilitic disease processes. The Wassermann reaction is by no means a constant manifestation which is lasting and unchanging in the individual syphilitic infection, like a stigma or a brand-mark. Its positivity comes and goes and comes again, and again disappears, etc. In other words, the positivity of the Wassermann reaction behaves, in its appearances and disappearances, like all the manifestations in the life of the syphilitic individual which we call syphilitic symptoms.

The question is, then, Is the Wassermann reaction perhaps nothing more than a syphilitic symptom? The answer will place the practical meaning of the serologic blood test in the right light.

If the reaction is truly nothing but a symptom, it should be influenced by antisyphilitic treatment. That it is so influenced is abundantly attested. In this connection and in regard to the symptoms of syphilis in general, the fact is to be emphasized that the earlier the treatment is begun and the more energetically it is carried out, the surer and easier it is to cause the reaction to change. The later the stage in which treatment is begun, the more refractory is the disease to the influence of treatment.

If then, Jesionek argues, one admits that the positivity of the reaction can be removed by therapeutic measures, that it is a symptom of syphilis,

that is, a sign of a constitutional-syphilitic condition, one should not be surprised by the irregular behavior of the reaction, especially in the primary stage in which it is now positive, now negative.

If we seek the explanation it will be found that the reaction is negative in the majority of cases during the earlier period of the existence of the primary lesion, but that as the end of the second incubation period is approached it all at once becomes positive; that is, eight to ten weeks after the infection. It is an accepted fact that it takes a variable length of time after the infection and the appearance of the primary lesion for the spirochetes to spread throughout the body from the place of infection. When this generalization of the virus is accomplished the reaction, for the first time, becomes positive. Although on the average this positivization takes places eight to ten weeks after infection and after the primary lesion has appeared, an occasional case is encountered in which the positive reaction precedes the appearance of the primary lesion. In such instances the systemic invasion antedates the first local symptom.

It is the individual factors resident in each individual which determine the type of the syphilitic disease and the character of its course. The protean character of the syphilitic picture is the consequence of the varying reactive conditions in the different patients. Moreover, if the reaction is regarded in the light of a symptom, it is easy to understand this variability, for syphilis has no symptom so characteristic as to be indispensable. For example, there have been cases which lacked glandular manifestations; cases in which there was no outbreak on the skin or the mucous membranes, and cases even of recent syphilis with healthy offspring.

From the foregoing, the conclusion is, that "The occurrence of a positive Wassermann reaction is to be regarded as neither more nor less than a symptom of syphilis which is not limited to a single phase of the disease process, but a symptom which may make itself manifest so soon and so long as active virus exists in the organism." The complement fixation reaction has demonstrated the truth of the clinical observation that the changes in the blood of syphilitics, on which the reaction is based, are referable, on the one hand, to the vitality and the activity of the spirochetes, which cause the disease, and, on the other hand, to the reactive processes on the part of the organism.'

In summing up, Jesionek says that "the Wassermann reaction has refined the technic of the diagnostic tests and thereby enabled us to demonstrate the syphilitic poison in cases in which our previous methods of research left us in the lurch. We are no longer obliged to await the appearance of the grosser changes in the skin or in the other organs to recognize the fact that the syphilitic poison threatens the health and the life of a patient. In cases of doubtful diagnosis the positive result of

the Wassermann reaction suffices for the decision. If we already suspect the specific nature of an affection on clinical grounds we remember, in regard to the positivity of the Wassermann reaction, that undoubted syphilitic symptoms are also "so good as regularly" accompanied by a positive Wassermann reaction. Naturally, the same rule holds in regard to the symptom of the positivity of the reaction as applied to every other syphilitic symptom: a single symptom, by itself, is never absolute proof. The positivity of the Wassermann reaction is not pathognomonic in the strict sense of the word. For that matter, neither is a macular eruption. When, however, we bring all the suspicious appearances together each single symptom gains in importance. "Of all symptoms which compose the picture of syphilis the Wassermann reaction is perhaps the most reliable."

As regards its relation to prognosis, Jesionek is of the opinion that "lies the infection never so far in the past, the Wassermann reaction is the sign that the patient is syphilitic." He then goes on to state that the reaction yields as little information concerning infectiousness as does the presence of a periostitis or a gumma. A positive reaction by no means indicates that the patient must transmit his syphilis to his children. Neisser is quoted to the effect that a positive reaction does not, of itself, demand that marriage shall be forbidden, as often in such cases the parents beget healthy children and themselves never again manifest a trace of the disease. If at least four years have passed since the infection, if during this period satisfactory treatment has been given and if there has been no symptom during the last year at least, marriage must be permitted. Nevertheless, as long as the Wassermann reaction remains positive no one can guarantee that some form of the syphilitic disease may not manifest itself in the offspring.

TREATMENT

As regards the treatment of syphilis, the physician no longer waits for the appearance of undoubted macroscopic symptoms, but begins treatment immediately on the first appearance of the Wassermann reaction. This is directly in line with the statement previously made that the earlier in the course of the disease treatment is instituted the easier it is to overcome the infection.

Discussing the old question as to the proper time at which to begin systemic antisyphilitic treatment, Jesionek states that the latest, although sparse, experiences seem to indicate that it is senseless to saturate the organism with mercury so long as the reaction is negative.

The failure of so-called preventive treatment when the evidence of the generalization of the virus is lacking seems to indicate that mercury has not in itself the power to kill or to paralyze the parasite. It does, however, possess the ability to aid the organism in its struggle. It is

only after the organism has itself begun to fight that external remedies are able to play an active part. The reactive process which we call the specific-disease-symptoms is evidence that the organism is working in its own defense. Therefore, the time to institute general treatment is that time in the primary stage when the Wassermann reaction first becomes positive.

Unfortunately, although the positive reaction may be changed to a negative through therapeutic measures, it is not possible to affirm with certainty that a cure has been attained as, in spite of a negative reaction, the poison may still remain in the organism.

RECAPITULATION

The chief points brought out by this summary of the literature on the Wassermann reaction are, in their order, as follows:

The Wassermann reaction gives a positive guide in the presence of *active* cutaneous manifestations, but is not entirely convincing when the cutaneous symptoms are dubious or lacking.

The Wassermann reaction is not specific for syphilis. It is positive more or less frequently in a considerable number of other diseases.

The technic is so exceedingly difficult and the sources of error so numerous as to render acceptance of results reported dependent on the qualifications possessed by the maker of the test.

The statistics at hand seem to show that the test responds positively in only about 50 per cent. of the total cases.

Therefore, the fundamental conclusion is drawn that the negative reaction has no diagnostic value.

Considered from the point of view of the period of disease, the reaction does not become positive in the primary stage until after a considerable lapse of time; usually eight to ten weeks from the time of the infection. Occasionally, it occurs as early as the third week. During the secondary period, when the activity of the disease is at its height, the reaction is positive with scarcely an exception. The positive reaction is considerably less frequent in the tertiary period, considered as a whole, although, in the presence of undoubted syphilitic symptoms, it is quite constant.

The same laws govern the behavior of the Wassermann reaction in congenital syphilis as in acquired syphilis.

Syphilitic parents with a positive Wassermann reaction may bear children with no trace of the disease and with a persistently negative reaction; or may bear children with no clinical signs of disease, but giving a positive reaction.

The mothers of syphilitic children are immune because, according to the Wassermann reaction, they are themselves syphilitic.

Periods of latency occur during the course of syphilis when no clinical signs of disease can be discovered. The reaction is positive less frequently

during these "latent" periods than during the periods of activity, especially if the "latency" occurs late in the course of the syphilitic disease.

The percentage of positive reactions found during the period of "late latency" agrees very closely with the percentage of cases undetected during life, but demonstrated at the autopsy to be syphilitic.

"Latency" may be due to cure (when the symptoms of disease never recur) or to "slumber" (when for some as yet unknown reason manifestations may unexpectedly develop at some future time). The Wassermann reaction does not distinguish between the negative reaction resulting from cure and the negative reaction from an infection which merely "slumbers."

The fact that the reaction, negative in the "latent" period, promptly becomes positive when the infection again becomes active, is very suggestive.

It follows from the statements above that the Wassermann reaction is not a constant and invariable accompaniment of the syphilitic disease process, but comes and goes just as do the other individual manifestations of the infection.

The Wassermann reaction is to be regarded as neither more nor less than a symptom which manifests itself in the presence of active disease processes regardless of the stage of the disease. In other words, it is not the period of the disease on which the occurrence of the complement fixation depends, but on the activity of the invading parasite.

When the Wassermann reaction is positive, but lacks clinical confirmation, the suggestion of the existence of a syphilitic process is exceedingly strong, but not absolutely beyond debate. When, however, the reaction is positive in the presence of manifest, or even merely suspicious, symptoms, the doubt is changed to a practical certainty by the fact of its occurrence.

Notwithstanding the statement just made, the tendency is to regard the occurrence of a positive reaction as positive evidence of the existence of active syphilis even when lacking confirmatory evidence.

A negative Wassermann test is of no value in prognosis. Apparently, the persistence of the positive reaction under certain conditions has no more value than the negative, as was shown in the discussion of the relation of the test to marriage.

Although the aim from a therapeutic point of view is to convert a positive reaction into a negative, so far as the Wassermann reaction is concerned, we cannot say whether the invading spirochetes have actually been conquered or only temporarily paralyzed. In short, our understanding of the inner meaning of the Wassermann reaction is incomplete and practically limited to the positive phase of the question. But our knowledge of even the positive phase lacks perfection.

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BLOOD-CULTURES DURING LIFE IN INFANTS AND YOUNG CHILDREN, WITH DESCRIPTION OF A NEW TECHNIC *

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Blood cultures made during life in young infants may be an aid to diagnosis or to prognosis, or they may be useful in the study of a given disease from the purely scientific standpoint, with a view to an ultimate practical or therapeutic application. In either case a safe and simple technic is a matter of necessity. It is probably true that the difficulties hitherto encountered in obtaining blood from young infants in quantities sufficient to make the cultural results of value are responsible for the lack of application of the measure in routine practice. The literature on the subject is very meager and is confined almost entirely to cultures taken from older children. In Churchill and Clark's¹ series of sixty-three blood cultures taken from children during life, only nine were under 2 years of age and none was under 12 months. They obtained the blood from a vein in the arm, as did Rotch and Low,² whose series does not include any infant less than 2 years old. Delestre³ obtained 1 to 2 c.c. of blood from the great toe after disinfecting and incising the skin. His studies were made on forty infants ranging from a few days to 4 years of age. Slavyk⁴ took the blood from the lobe of the ear, using only a few drops to make the cultures. Neither one of these methods is above criticism, and to enter a vein at the elbow without exposing the vessel by incision is a matter of impossibility in all but a very small number of young infants, whether they are well or poorly nourished. We believe that the method followed by us is an improvement on any which has been previously reported, and therefore the details of the procedure are given.

*From the Pathological Laboratory of the Babies' Hospital.

1. Churchill and Clark: *AM. JOUR. DIS. CHILD.*, 1911, i, 193

2. Rotch and Low: *Jour. Am. Med. Assn.*, 1907, xlviii, 185

3. Delestre: *Ann. de gyn. et obst.*, 1901, lv, 51.

4. Slavyk: *Jahrb. f. Kinderh.*, 1901, liii, 505.

TECHNIC

The blood was taken from the external jugular vein in all the cases in the series except three. In the three exceptions the vein chosen was the superficial temporal in two cases and the median basilic in one.

The patient having been tightly wrapped in a sheet to secure the arms at the sides and prevent struggling, was placed on a table. The head was turned to one side, hyperextended over the end of the table and supported in that position by an assistant. This served the double purpose of making the site of operation more accessible and of facilitating the direct introduction of the needle by tightening the skin over the vein.

The operator's hands were sterilized in the usual manner. The site of aspiration was washed with alcohol and dried, after which tincture of iodine was applied and allowed to remain for three minutes. In few cases was the vein so obscured as to necessitate the removal of the iodine before puncture. The entrance into the vein was most readily effected during a paroxysm of crying when the vessel was distended. Digital pressure above the clavicle we have found to be practically valueless in increasing the prominence of the vein.

A 2-c.c. Luer syringe was used with a 22-gauge needle 1.5 cm. in length. The needle was inserted into the vein in the direction of the blood current and 1 c.c. of blood was drawn off and transferred directly to 30 c.c. of bouillon. It is important that the concentration should not be greater than one in twenty or thirty in order to avoid bactericidal action of the blood. Broth of a reaction of + 0.5 per cent. of phenolphthalein was used in making these cultures and we believe that fluid media give better results than do solid ones.

Three points in the technic are worth emphasizing: the iodine should remain on for at least three minutes before puncture; the puncture should be performed through the iodine whenever possible; it is essential that the vessel be entered with the least possible manipulation in order to avoid contamination from the deeper layers of the skin.

Failures are encountered rarely. With a little practice it is surprising how few attempts end unsuccessfully provided a vein is distinctly visible. There are, however, exceptional cases, usually fat, well-nourished babies, in which the vein is completely obscured by the subcutaneous fatty tissue. None of the children showed any ill effects attributable to the operation, and hemorrhage in the form of a hematoma was not encountered unless the needle transfixes the vessels. The size or prominence of the vein is seemingly not dependent on the age of the child. The small marasmus babies as a rule had prominent veins, whereas difficulties were sometimes encountered in the older, well-nourished children.

The ages of the children in the series varied from 10 days up to 4 years; sixteen children, or 20 per cent., were under 6 months old; twenty-three, or 28.7 per cent., were between 6 months and 1 year; twenty-one, or 26.3 per cent., between 1 and 2 years; four children, or 5 per cent., were between 2 and 3 years old; and sixteen, or 20 per cent., were over 3 years of age. Two babies were only 10 days old, and nearly half the children studied were under 1 year of age, while 75 per cent. were under 2 years. One hundred cultures were made on eighty children. Twenty-six cases, or 32.5 per cent., gave positive results, while fifty-four cases, or 67.5 per cent., gave negative cultures.

The clinical diagnosis varied as Table 1 shows.

LOBAR PNEUMONIA

There are thirteen cases of lobar pneumonia in our series, in four of which the pneumococcus was found in the blood, accompanied in one instance by *Bacillus influenzae*. All of the thirteen children recovered, so that the blood-cultures were of no prognostic value in this series. All four positive cultures were obtained before the crisis, though in six of the negative cases the blood was also taken while the temperature was still high. None of these patients developed empyema or any other complication. Otten⁵ found the pneumococcus in the blood in nine of the seventy cases of lobar pneumonia studied in older children. Of the nine positive cases five children died and four recovered. Churchill and Clark found four positive cases among fifteen lobar pneumonias examined. In two of our positive cases the patients were 9 months old, one was 17 months and one was 3 years of age.

The case of the child whose blood contained both pneumococci and influenza bacilli is of interest. He was 9 months old. On the fourth day of the disease his blood gave a negative culture; on the ninth day it was found to contain both organisms, and on the twelfth day it was negative again. His crisis came on the fourteenth day and the child recovered without complications. This fact is especially interesting because the influenza bacillus isolated from his blood was virulent for rabbits, proving that influenzal bacteriemia of pulmonary origin may be due to a virulent strain of *B. influenzae* and may run its course without the occurrence of meningitis. Thus Cohen's⁶ separation of the influenza bacillus from the *Bacillus meningite cérébrospinale septicémique* would seem to be unnecessary. Influenza bacilli were also isolated from the bronchial secretion of this infant.

5. Otten: *Jahrb. f. Kinderh.*, 1909, lxi, 568.

6. Cohen: *Ann. de l'Inst. Pasteur*, 1909, xxiii, 273.

TABLE 1.—SHOWING BLOOD CULTURES IN A VARIETY OF DISEASES

Case No.	Age, Months	Sex	Diagnosis	Organism Found	Results
1	30	F	Malignant endocarditis	Streptococcus	Died
2	7	M	Broncho-pneum. and meningit.	Streptococcus	Died
3	9	M	Broncho-pneum. and empyema	0	Died
4	1/8	M	Meningeal hemorrhage	0	Died
5	9	M	Lobar pneum. and septic arthr.	Pneumococcus	Cured
6	19	F	Septic arthritis and meningitis	Streptococcus	Died
7	48	M	Lobar pneum. and empyema	Pneumococcus	Cured
8	7	M	Broncho-pneumonia	0	Died
9	11 1/2	F	Epidemic meningitis	0	Cured
10	42	M	Lobar pneumonia and empyema	0	Cured
11	18	F	Broncho-pneumonia	0	Died
12	2	F	Broncho-pneum. and empyema	Streptococcus	Cured
13	36	F	Lobar pneumonia	0	Cured
14	5	F	Retropharyngeal abscess	0	Died
15	18	M	Double empyema	Pneumococcus	Died
16	15	M	Broncho-pneumonia	Pneumococcus	Cured
17	4 1/2	M	Broncho-pneumonia	0	Died
18	36	F	Lobar pneumonia	Pneumococcus	Cured
19	24	M	Lobar pneumonia	0	Cured
20	22	M	Lobar pneum. and empyema	Pneumococcus	Died
21	6	F	Erysipelas	Streptococcus	Died
22	18	F	Broncho-pneumonia	0	Died
23	8	F	Tuberculous meningitis	0	Died
24	54	F	Tuberculous meningitis	0	Died
25	2 1/2	M	Broncho-pneum. and empyema	Pneumococcus	Died
26	36	M	Exacerbation of old endocarditis	0	Improved
27	5	M	Tuberculous meningitis	0	Died
28	14	F	Lobar pneumonia	0	Cured
29	13	F	Broncho-pneumonia	0	Died
30	42	M	Chorea	0	Cured
31	9	M	Septic arthritis of hip	0	Cured
32	8 1/2	F	Marasmus and nasal diphtheria	Klebs-Loeffler Bac.	Died
33	15	M	Broncho-pneumonia	0	Cured
34	36	M	Congenital heart malformation	0	Unimproved
35	42	F	Rheumatic endocarditis	0	Died
36	36	M	Pulmonary tuberculosis	0	Unimproved
37	48	F	Rheumat. endo- and pericarditis	0	Died
38	13	F	Empyema	Pneumococcus	Cured
39	42	M	Empyema	0	Cured
40	8	F	Acute nephritis	0	Died
41	10	F	Broncho-pneum. and pertussis	0	Unknown
42	14	M	Lobar pneumonia	0	Cured
43	8	M	Pneumococcus meningitis	Pneumococcus	Died
44	11	M	Broncho-pneum. and measles	0	Died
45	17	M	Lobar pneumonia	Pneumococcus	Cured
46	16	M	Lobar pneumonia	0	Cured
47	9	M	Lobar pneumonia	Pneumococcus and <i>B. influenza</i>	Cured
48	3	F	Pertussis	0	Unknown
49	2 1/2	M	Broncho-pneumonia	0	Cured
50	15	M	Broncho-pneumonia	0	Died

TABLE 1.—Continued

51	20	M	Broncho-pneumonia	0	Died
52	17	F	Broncho-pneumonia	0	Cured
53	2½	M	Marasmus and furunculosis	Pneumococcus	Cured
54	6	M	Pleuropneum. and meningitis	Pneumococcus	Died
55	5	F	Empyema and meningitis	Pneumococcus	Died
56	3	F	Marasmus	0	Improved
57	4	F	Acute bronchitis	0	Cured
58	12	F	Broncho-pneumonia	0	Died
59	12	M	Broncho-pneumonia	0	Cured
60	½	M	Pyemia and septic arthritis	Aurococcus	Died
61	6	F	Lobar pneumonia	0	Cured
62	10	F	Broncho-pneumonia	Pneumococcus	Cured
63	36	M	Broncho-pneumonia	Pneumococcus	Cured
64	36	M	Lobar pneumonia	0	Cured
65	42	F	Broncho-pneumonia	0	Cured
66	7½	M	Broncho-pneumonia	0	Cured
67	8	M	Gastro-Intes. intox. and broncho-pneumonia	0	Died
68	6	M	Marasmus	0	Died
69	14	F	Broncho-pneumonia	0	Cured
70	7	M	Broncho-pneumonia	0	Cured
71	9	M	Broncho-pneum. and tetany	0	Cured
72	24	M	Broncho-pneum. and empyema	0	Cured
73	5	M	Empyema and meningitis	Pneumococcus	Died
74	24	M	Lobar pneumonia	0	Cured
75	2	M	Broncho-pneumonia	Streptococcus	Died
76	15	F	Lobar pneum. and empyema	Pneumococcus	Died
77	2	F	Marasmus and cellulitis of scalp	0	Unimproved
78	10	F	Broncho-pneum. and von Jaksch Anemia	0	Unimproved
79	60	M	Empyema	0	Cured
80	18	M	Lobar pneumonia	0	Cured

TABLE 2.—RESULTS OF BLOOD-CULTURES IN LOBAR PNEUMONIA

Case No.	Age, Months	Sex	Day of Positive Cult.	Day of Negative Cult.	Day of Crisis	Organism	Result
5	9	M	*	Pneumococcus	Cured
13	36	F	5th	?	0	Cured
18	36	F	6th	17th	11th	Pneumococcus	Cured
19	24	M	5th	5th	0	Cured
28	14	F	8th	11th	0	Cured
42	14	M	7th	9th	0	Cured
45	17	M	21st	23rd	22nd	Pneumococcus	Cured
46	16	M	6th	7th	0	Cured
47	9	M	9th	4th and 12th	14th	Pneumococcus and <i>B. influ.</i>	Cured
61	16	F	5th	7th	0	Cured
64	36	M	8th	8th	0	Cured
74	24	M	2d, 4th, 7th	3rd	0	Cured
80	18	M	3d, 4th	4th	0	Cured

*Day of onset unknown.

TABLE 3.—RESULTS OF BLOOD-CULTURES IN BRONCHO-PNEUMONIA

Case No.	Age, Months	Sex	Day of Positive Culture	Day of Negative Culture	Organism	Result
2	7	M	2nd	Streptococcus	Died seventh day.
8	7	M	8th	0	Died tenth day; no autopsy.
11	18	F	2nd	0	Died at home; date not known.
16	15	M	8th	20th	Pneumococcus	Cured.
17	4½	M	9th	0	Died tenth day; heart's blood sterile.
22	18	F	2nd	0	Died second day; no autopsy.
29	13	F	15th	0	Died nineteenth day; heart's blood sterile.
33	15	M	6th	0	Cured.
41	10	F	4th	0	Left hosp. and could not be found.
44	11	M	7th	0	Died, no autopsy.
49	2½	M	8th	0	Cured.
50	15	M	1st	0	Died second day; heart's blood sterile.
51	20	M	9th	0	Died; no autopsy.
52	17	F	5th	0	Cured.
54	6	M	12th	Pneumococcus	Died fourteenth day; no autopsy.
58	12	F	11th	0	Cured.
59	12	M	6th	0	Cured.
62	10	F	7th	17th	Pneumococcus	Cured.
63	36	M	3rd	11th	Pneumococcus	Cured.
65	42	F	15th	0	Cured.
66	7½	M	1 month after onset	0	Cured.
69	14	F	15th	0	Cured.
70	7	M	7th	0	Cured.
71	9	M	21st	0	Cured.
78	10	F	4th	0	Cured.
75	2	M	4th	Streptococcus	Died.

TABLE 4.—RESULTS OF BLOOD-CULTURES IN EMPYEMA

Case No.	Age, Months	Sex	Day of Positive Culture after onset of Pneumonia	Day of Negative Culture	Organism	Result
3	9	M	15th	0	Died thirtieth day; blood at autopsy streptococcic.
7	48	M	26th	28th	Pneumococcus	Cured.
10	42	M	28th	0	Cured.
12	2	F	9th	Streptococcus	Cured.
15	18	M	26th and 30th	40th	Pneumococcus	Died eight weeks after onset of pneumonia.
20	22	M	21st	18th	Pneumococcus	Died twenty-seventh day. Heart's blood at autopsy pneumococcic.
25	2½	M	14th*	Pneumococcus
38	13	F	8th	11th	Died five weeks after onset pneum.
39	42	M	10th	Pneumococcus	Cured.
55	5	F	Over 3 weeks	0	Cured.
72	24	M	2 months	Pneumococcus	Died same day.
73	5	M	16th	0	Improving.
76	15	F	4th and 6th	Pneumococcus	Died same day.
79	60	M	21st	Pneumococcus	Died. No autopsy.
					0	Improving.

*Nineteen days before empyema was discovered.

BRONCHOPNEUMONIA

Twenty-six cases of bronchopneumonia were studied, with six positive results. The pneumococcus was found four times and the streptococcus twice. Both children with streptococcus and one with pneumococcus infection died, while three pneumococcus patients recovered. The cocci were found in the blood on the second, fourth and twelfth days in the fatal cases and on the third, seventh and eighth days in the patients who recovered. So that no prognostic value could be ascribed to the date of positive blood-cultures in these twenty-six cases. Eight of the children in the negative series died, a slightly lower mortality-rate than obtained in the positive cases. Churchill and Clark found the pneumococcus in one of three lobular pneumonia cases.

EMPHYEMA

Fourteen children with empyema gave positive blood-cultures nine times; in all but one the pneumococcus was the bacterium found. Six children among the positive cases died, while only one of the negative cases resulted fatally. Three of the infants with positive cultures had pneumococcus meningitis as well as empyema. It would seem, then, that bacteriemia in this series of empyema patients was a bad prognostic sign in about 55 per cent. of the cases, and that it sometimes meant infection of another serous membrane. The single example of streptococcus empyema in this series of cases recovered. The subject was a baby only 2 months old. It is probable that all these cases of empyema followed pneumonia, but as the majority of them were admitted with pus in the chest it was not always possible to diagnose the type of pneumonia preceding the pleurisy. Bronchopneumonia was present in five children, lobar pneumonia in four and in five cases the type was not diagnosed. Four of the children with bronchopneumonia died, only three having given a positive blood-culture; while of the empyema cases following lobar pneumonia two children died, both having had a pneumococcus bacteriemia.

MENINGITIS

Six cases of meningitis included three of the tuberculous form, one of the meningococcus, one of the pneumococcus, and one of the streptococcus varieties. The last two gave positive blood-cultures; the other four did not. The child with meningococcus meningitis recovered after treatment with antimeningococcus serum. All the rest were fatal, as was to be expected, the meningitis being the terminal lesion in a general infection.

RHEUMATISM

There were four cases of rheumatism in children 3 and 4 years old. None gave a positive blood-culture though two children had acute endocarditis, one had an acute exacerbation of an old endocarditis, and one had chorea. Two patients died, but only one came to autopsy, and her heart's-blood after death gave no growth.

OTHER POSITIVE CASES

In one case of malignant endocarditis the child had a streptococcus bacteriemia and died on the twenty-fifth day of the disease.

A case of erysipelas gave a negative blood-culture on the sixth and seventh days of the disease, but on the eleventh day the streptococcus was found in the blood and the patient died on the seventeenth day.

The only case in which the aureococcus was found in the blood was a child 10 days old, who had been admitted with omphalitis and suppurative arthritis of the wrist from which the same organism was grown. The baby died.

Two marasmic infants are of interest. One had furunculosis. He was 2 months old and pneumococci were found in his blood though his temperature was normal at the time the culture was taken. He recovered. The other child was 8 months old and had nasal diphtheria. *B. diphtheriae* was found in pure culture in her blood. She died but no autopsy was permitted. The case will be reported in detail later.

SUMMARY

Blood for bacteriologic examination was readily obtained from the external jugular vein in infants as young as 10 days of age.

The pneumococcus was found before the crisis in the blood in four out of thirteen cases of lobar pneumonia (30.8 per cent.), all of which patients recovered.

A bacteriemia was demonstrated in six out of twenty-six cases of bronchopneumonia (23 per cent.), the pneumococcus being recovered in four and the streptococcus in two. Both streptococcus patients died and one pneumococcus case also proved fatal. In eight bronchopneumonia cases without bacteriemia the patients also died.

The highest percentage of positive blood-cultures was found in cases of empyema: nine of fourteen, or 64.3 per cent. But even in empyema bacteriemia does not necessarily mean a fatal prognosis, as in 33.3 per cent. of the positive cases the children recovered.

THE PANCREATIC FERMENTS IN INFANTS *

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For many years our lack of knowledge of the processes of intestinal digestion, and of the action of the glands which line the wall of the intestine, as well as those which pour their secretions into it, has hindered the study of the metabolic processes during infancy. It has frequently been regretted that we have to content ourselves with a direct study of the activities of the stomach, and cannot gain similar direct access for an investigation of the intestine, of the pancreas and of the liver. From time to time ingenious methods have been devised to overcome the inaccessibility of this region, and although most of these have proved of doubtful value, and hardly any have been satisfactorily applied to infants, it may be well to review them briefly.

The first methods were based on the principle of giving a food by mouth in such a form that it could not be digested by the stomach, and of subsequently examining the stool to judge of the efficiency of the intestinal digestion. Sahli's glutoid capsule and Schmidt's nuclear tests based on this principle were devised to test the tryptic activity of the pancreas. However, as it has been shown that the capsules are dissolved when given to dogs deprived of the pancreas,¹ and as Schmidt's test is also not reliable, the advisability of adapting these tests to our purposes may be dismissed.

A second method of investigation consists in examining the stool for the ferments themselves, especially for trypsin, but also for amylase, and for lipase or for the products of fat splitting. Many investigations have been carried out in this way to ascertain the secretion of trypsin. For this purpose the Müller-Schlecht² method, which depends on the digestion of serum, or the Volhard³ and Gross⁴ method, in which casein is substituted for serum, has been employed. A method of estimating the activity of intestinal diastase is also based on the above principles, and consists of a test introduced by Wohlgemuth⁵ to judge of the starch-converting power of the stool. Similarly, but with less success, the stools have been examined for lipase, but more frequently for their content of free fat, fatty

*From the Research Laboratory, Department of Health, New York City.

1. Frank, F.: Arch. f. Verdauungskr., 1912, xviii.

2. Schlecht, H.: München. med. Wehnschr., 1908, xiv, 725.

3. Volhard, F.: München. med. Wehnschr., 1907, 403.

4. Gross, O.: Arch. f. exper. Path. u. Pharmakol., 1908, lviii, 157.

5. Wohlgemuth, J.: Berl. klin. Wehnschr., 1910, p. 92.

acids and soaps. The Cammidge reaction of the urine, said to be a test for glycerin, a product of fat-splitting, may be passed over with mere mention.

Still another principle is involved in the test of Boldyreff.⁶ This consists in giving the patient oil by mouth, an oil-breakfast, which excites a regurgitation of pancreatic fluid into the stomach. The stomach contents are evacuated and tested for the pancreatic ferments. We have seen but one report of a test by this method on an infant, and in that case it was not successful.⁷ One of the difficulties is that the regurgitation from the duodenum does not always follow. Moreover, in infants, it would seem to be of doubtful value, on account of the necessity of putting a large amount of oil into the stomach.

One valuable source of information which has been grasped by those interested in this phase of physiology or pathology, is the occasional fistulæ of the pancreas or of the small intestine, which allow of the collection of their secretions. However, this exceptional opportunity, which has been taken advantage of from time to time since the famous observations of Beaumont in 1833, has never been accessible to those desirous of making a similar study on an infant.

The greatest advance in method has been made recently by the use of duodenal tubes. Almost simultaneously Gross⁸ and Einhorn⁹ published an account of a tube which when introduced into the stomach was carried by peristalsis into the upper intestine. Hemmeter¹⁰ had attempted to use this direct method some years before. By means of this direct method, Einhorn and Rosenbloom¹¹ made a study of pancreatic ferments in the adult, which will be referred to below.

About two years ago a duodenal tube modelled after the Gross tube was devised for use on infants, and the early part of this study was carried out with its aid. It was found, however, that the method could be modified and greatly simplified for infants; that a simple catheter could be employed for these examinations. This duodenal catheter has been described in the pages of this journal in connection with the diagnosis and treatment of pylorospasm,¹² and in a study of icterus neonatorum.¹³ It has also been briefly described in a paper on the bacteriology of the duodenum in infants,¹⁴ and elsewhere,¹⁵ so that it is unnecessary

6. Boldyreff, W.: *Zentralbl. f. d. ges. Physiol. u. Path. d. Stoffwechs.*, 1908, p. 209.

7. Ibrahim, J.: *Verhandl. d. Deutsch. Naturf. u. Aertzte*, 1908, p. 316.

8. Gross, M.: *New York Med. Jour.*, 1910, No. 2.

9. Einhorn, M.: *Med. Rec.*, New York, 1910, No. 3.

10. Hemmeter: Complete reference not supplied.

11. Einhorn, M., and Rosenbloom, J.: *Arch. Int. Med.*, 1910, p. 667.

12. Hess, A. F.: *AMER. JOUR. DIS. CHILD.*, 1912, p. 133.

13. Hess, A. F.: *AMER. JOUR. DIS. CHILD.*, 1912, p. 304.

14. Hess, A. F.: *Jour. Infect. Dis.*, July, 1912, p. 71.

15. Hess, A. F.: *Arch. Int. Med.*, 1912, p. 37.

here to enter into the technic of its use. The catheter was used in this study of the pancreatic ferments because it seemed certain that an advance in our knowledge could be made by means of this method, which must be of greater value than the indirect methods which have preceded it. Just as it is preferable to test for rennet and for pepsin the stomach contents rather than in the stool, so in the case of the pancreatic ferments it is preferable to examine the duodenal contents rather than the stool. In the stool we have leukocytic ferments, bacterial ferments and other cellular ferments which possess proteolytic activity and are readily confused with trypsin. Schlecht's² report of the digestion of serum by means of a solution of old, thoroughly dried stool would even suggest activity other than ferment action, as a cause of proteolysis. In addition to the fact that the pancreatic ferments are mingled with non-pancreatic ferments in the feces — for besides these cellular enzymes, many others, for example, intestinal lipase, erepsin and probably intestinal amylase appear in the stool — the material for examination must naturally be contaminated with unutilized food products. But of more weight is the fact that we have no means whatsoever of even estimating how much ferment has been absorbed or utilized in the small intestine. That this factor is large we can infer from our knowledge that this part of the intestine is the seat of the physiologic activity of these ferments, and that they must be largely used up in this process. Experiment confirms us in this opinion, for it has been demonstrated that the ferments of the pancreas are hardly present in chyme obtained from a fistula in the cecal end of the ileum.² Realizing this defect in method, and in order to allow as little time as possible for absorption, a cathartic is given before obtaining stools for the ferment tests.

Such are the criticisms which justly can be levelled at any tests of stool for pancreatic ferments, but which a direct duodenal test is not exposed to. However, the direct method which we have used in this study, like most methods, is likewise not perfect. It may truly be argued that the duodenal fluid may suffer an admixture of gastric juice. At present this cannot be obviated; however, if all duodenal fluid which is acid is discarded, and only alkaline or neutral juice examined, this objection loses much of its force. We should realize also that the pancreatic juice obtained in this way cannot be considered pure, as it contains bile as well as some succus entericus. These criticisms would apply forcibly were we pursuing a purely chemical study of pancreatic enzymes. However, we have not undertaken a study of this nature, but rather an investigation of the activity of duodenal digestion, in which the pancreatic ferments take a pre-eminent part, and the bile and other juices play a minor but by no means negligible rôle. Moreover, there is no other way in which a pancreatic juice even comparatively pure can be obtained.

When we inquire into the present status of our knowledge in regard to the activity of the secretions of these glands in infancy, we find that one of the most modern and exhaustive books on the physiology of the digestion of the infant, that of Czerny and Keller,¹⁶ confines itself largely to a discussion of the results of post-mortem investigations, "in view of the fact that the secretions of the intestinal glands and the functions of these secretions are not accessible to direct examination *intra vitam*." Tests of this nature, made with the watery extract of a gland, have a very limited application to the physiologic activity of an organ, and can be considered of only temporary value in lieu of something better. This becomes all the more evident when we reflect that merely the proferment may exist in the gland parenchyma, and that an activating substance, such as enterokinase in the case of trypsinogen, may be necessary to render the ferment potent. We shall have occasion to refer to these investigations based on post-mortem material, and also to those undertaken by means of the examination of the stool. There has been no direct test of the pancreatic ferments of infants.

TECHNIC OF CHEMICAL TESTS

The fluid was brought to the laboratory as soon as possible, generally within an hour or two and subjected to the following tests:

Amylase Test: One c.c. of duodenal fluid was added to a tube containing 10 c.c. of freshly prepared 1 per cent. starch solution, and 1 c.c. of toluol. A control tube contained only starch solution and toluol. Both were placed in the thermostat at 37 C. for forty-eight hours. The mixtures were then made up to 50 c.c. by the addition of water, and run from a burette into 10 c.c. of Fehling's solution (Fehling's solution equals 5 c.c. of the alkaline solution, plus 5 c.c. of the copper solution, plus 30 c.c. water). Ten c.c. of this solution represents 0.002 gm. of glucose. As an indicator of the complete reduction of the Fehling's solution concentrated potassium ferrocyanid (2 to 3 c.c.) and glacial acetic acid (a few drops) were used.

Lipase Test: One c.c. of the duodenal fluid was added to 1 c.c. neutral ethyl butyrate, 1 c.c. toluol, 10 c.c. water. As controls a test of the duodenal fluid and one of the ethyl butyrate were made. The three tubes were incubated for twenty-four hours, and titrated against N/20 NaOH, using phenolphthalein as an indicator. The acidity of the duodenal fluid, and of the butyrate solution, was then deducted to obtain the net amount of acid due to lipolytic action.

Trypsin Test: In the early tests made over a year ago Mett's tubes were used. As is well known, these consist of tubes of small caliber containing coagulated egg-white. These were found serviceable for qualitative tests, but unreliable for quantitative estimations. It was found that tubes of 5 per cent. gelatin were fully as reliable and much more practicable, so that this method was followed in most of the tests. To a tube of gelatin 0.5 c.c. of duodenal fluid, 0.5 c.c. of toluol, as well as 0.25 c.c. of N/1 NaOH were added. The control consisted of a tube containing gelatin, sodium hydrate, and toluol. Tubes prepared in this way were incubated generally for twenty-four and for forty-eight hours, and then placed in the refrigerator. The time necessary for liquefaction was noted, and

16. Czerny, A., and Keller, A.: *Des Kindes Ernährung*, etc., 1906, i, 66.

also whether this change was complete or incomplete. Casein was not used in these tests as it is well known that it is reacted on by erepsin as well as by trypsin.

In addition to these chemical tests the amount, the color, the consistency and the reaction of the fluid to litmus and to phenolphthalein were noted. At the time of the passing of the catheter, the amount of the stomach content, its reaction to litmus and to Congo paper, were recorded, as well as various secretory and motor phenomena.

SCOPE OF ORIGINAL INVESTIGATION

The following direct study of pancreatic ferments by means of the duodenal fluid may be grouped thus:

1. Normal cases:

- a. Tests before the infant had nursed (during first half day of life).
- b. Tests during first week of life.
- c. Test on older infants (one week to one year).

2. Pathological cases:

- a. Tests in cases of marasmus (atrophy, decomposition).
- b. Tests in cases of pylorospasm associated with gastric hypersecretion.

3. Chemical and physiologic observations on the duodenal secretion.

1. *Normal Cases.*—*a. Tests of Unfed New-born Infants.*—The first tests were carried out on infants varying in age from a few weeks to a few months, but it soon became evident that in order to get a comprehensive view of the subject, the ferments ought to be sought from the day of birth, even before they had been put to the breast. Accordingly, a large number of infants were examined by means of the catheter during the first few hours of life, to ascertain whether the pancreatic ferments are present in the duodenum at this period and whether they are secreted independently of the stimulus of colostrum. The passage of the catheter in the new-born is very easily accomplished, as has been recently pointed out in an article on icterus neonatorum. The two investigations were pursued simultaneously; that is to say, the fluid which was aspirated was considered both in regard to the presence of bile and the pancreatic ferments. The examination was by no means always successful, for although access to the duodenum was almost always possible, frequently the upper intestine was empty and no fluid could be aspirated. In a few instances, in these very young infants, a slight admixture of blood rendered the fluid valueless for our purposes; and in some other cases the scanty duodenal contents were rendered acid by an admixture of gastric juice. For these various reasons, although fifty-five tests of the "unfed new-born" were attempted, duodenal juice was obtained in only eleven, and in no instance

in sufficient quantity to make tests for all three ferments, for trypsin, lipase and amylase. However, a test for one ferment was made in one case, and for another in the next, using all the ferment that was secured, with the object of ascertaining whether these pancreatic ferments are present in the intestine before the ingestion of any food.

Before proceeding to detail the results, it will be of advantage to review the previous work in this field; and as the investigations on this group of infants, those who had not nursed, are so few in number, it would seem advisable at the same time to include reports of infants who were somewhat older. The greatest divergence of opinion has always existed as to the time of appearance of amylase. Zweifel,¹⁷ who made use of extracts of the pancreas, failed to demonstrate the ferment in infants under two months of age, and Korowin¹⁸ confirmed these results. Moro,¹⁹ however, repeating this investigation, but making use of an improved technic, more especially by extracting the pancreas for a longer period and at a higher temperature, demonstrated the presence of diastase in the pancreas of an infant which died at birth, and of some others which had lived for a few days. Ibrahim⁷ found amylase in the pancreas of the new-born and of the premature infant, and numerous ferments in the meconium.

As is well known, trypsin is not present in the pancreas, but exists in the form of its proferment, trypsinogen, which is activated by the enterokinase of the intestine. Both trypsinogen and enterokinase have been found in the fetus, and trypsin in the stools during the first day of life.²⁰ Another proteolytic ferment, erepsin, which we shall have occasion to refer to later, has likewise been found in the fetus.²¹

Lipase has been demonstrated in the meconium in small amounts during the first day of life,²⁰ and, according to Sedgwick,²² a gastric lipase of considerable lipolytic power may be obtained from the stomach by the second week.

It will be noted that most of these examinations have been made either on post-mortem material, or on infants somewhat older than those comprising our first group. In our experience trypsin and lipase were found most constantly. The former in nine out of eleven tests, and by no means as a mere trace, but sufficient frequently to digest the gelatin in twenty-four to thirty-six hours. Lipase was demonstrated in four of the five tests, also in considerable quantity—from 0.5 c.c. to 2.9 c.c.—as measured by titration with 1/20 N. NaOH solution. Lipase of uncertain origin

17. Zweifel: *Untersuch. u. d. Verdauungsapparat d. Neugeb.*, 1874, p. 35.

18. Korowin, J.: *Jahrb. f. Kinderh.*, 1875, viii.

19. Moro, E.: *Jahrb. f. Kinderh.*, 1898, iii, 342.

20. Hecht, A.: *Die Faeces d. Säuglings*, 1910, p. 153.

21. Langstein, M. and Soldin, M.: *Jahrb. f. Kinderh.*, 1908, p. 9.

22. Sedgwick, J.: *Jahrb. f. Kinderh.*, 1906, p. 194.

was found in small amount in the stomach contents. Amylase was present twice and absent six times. This positive reaction was not due to an admixture of saliva, for no saliva was present in the material examined; the one case belonged to a series of four, in which a dilute solution of alum was swabbed on the papillæ of the salivary ducts, resulting in complete inhibition of salivary excretion. From these tests we conclude that the three pancreatic ferments are frequently present in the duodenum at or soon after birth. The youngest infant in which amylase was demonstrated was one and a half hours old.

The results of these tests, comprising a narrow field, are of physiologic rather than of clinical interest, and need no clinical commentary. The accepted mechanism of pancreatic secretion is that secretin is elaborated by the mucosa of the small intestine, enters the portal circulation and acts as a hormone to stimulate the pancreas. There is no way of judging whether secretin, in our cases, acted as the messenger to stimulate the pancreatic activity; it has been found in infants which died at birth, but it is not at all times present in the intestine of the new-born. Whatever the mechanism, it is clear that food is not needed to stimulate the activity of the pancreas. The hydrochloric acid which is regularly present in the stomach at birth, as we shall show at another time, would seem to be sufficient to initiate the excretion of pancreatic juice into the duodenum.

b. Tests During the First Week of Life.—Fifty tests were made on thirty-three infants varying in age from one-half to seven days, the same method of examination being employed as in the cases of the former group. Some of these tests did not include an analysis of the duodenal contents, but were made for the purpose of obtaining gastric juice or bile, of determining the state of the pyloric sphincter, or to obtain material for bacteriologic investigation. However, in forty-one instances one or more of the three pancreatic ferments were investigated. As was to be presupposed from our experience with the younger infants, the presence of all three ferments was demonstrated. Trypsin was regularly found in quantity sufficient to digest 5 per cent. gelatin within twenty-four hours; in only two of nineteen tests was it absent. Through an error, 10 per cent. gelatin was used for several of these tests, and as gelatin in this concentration is not applicable as a test for trypsin, these examinations were necessarily discarded.

Lipase was found in all of the ten fluids in which it was tested. In infants one week of age the duodenal juice obtained within an hour is insufficient in amount to carry out the tests with each fluid, for 2 c.c. are necessary for the lipase test, one for the amylase test, and 1.0 c.c. for trypsin. If only a small amount of fluid was obtained, trypsin was tested for, but unless the fluid was neutral or alkaline to litmus, it was not examined for ferments. The lipase varied in quantity from 0.25 c.c. to

2.4 c.c., almost all being under 2.0, as judged by titration with 1/20 N. NaOH.²³ It is not possible to ascribe this variation solely to a difference in the quantity of lipase secreted, as the fluids examined were not sufficiently pure to allow of this deduction. In addition to a difference in the amount of lipase, there are numerous factors which may well have contributed to these varying results. For instance, the dilution of the pancreatic lipase with succus entericus or with gastric juice; the presence of more or less bile, which would tend to dilute the pancreatic secretion, although at the same time augmenting its lipolytic action; the variation in the reaction of the juices. Experiments undertaken at the outset of this work clearly demonstrated that a slight addition of Na_2CO_3 or of NaOH to the fluid was sufficient to alter its ferment action. In view of these facts it seems advisable, for the present at least, to consider these tests from a qualitative rather than from a quantitative point of view. Nevertheless the difference in lipase is so great that we seem justified in concluding that in infants of this age there is a marked normal variation in its activity.

Amylase was tested for in nineteen cases and found in every instance. It was present in larger quantity than in the cases of group *a*, and in several instances completely reduced the starch solution. Some cases could not be tested for amylase on account of the admixture of saliva to the fluid. However, that saliva did not account for the amylolytic reaction is proved by the fact that in numerous instances the stomach contents failed to reduce starch, whereas the duodenal fluid possessed this activity, and by two instances in which the secretion of saliva was once more inhibited by a local application of alum.

c. Tests On Older Infants.—The group of older infants comprises twenty tests carried out on fourteen infants, varying in age from two weeks to one year. As we had already determined that all the ferments are present in very young infants, these examinations were studied with the purpose of ascertaining possible quantitative differences in the amount of juice obtained, or in the potency of the ferments, compared to that of infants during the first week of life, or of defining a relationship between the composition of the food and the secretion of the three ferments. These infants were of about normal weight; we could not, however, be certain in many cases that they had not at a previous time suffered from intestinal disturbances. Two were nursing babies, the others fed in most instances with a mixture of milk, containing approximately 2 per cent. fat, 6 per cent. sugar and 2 per cent. protein. This group should have included a large number of healthy breast-fed babies, but it was not possible for us to obtain many normal nurslings for this examination, so

23. In giving figures of the amounts of the ferments we realize that they do not represent a quantitative estimation of the ferments but merely denote its activity.

that an extension of this test had to be deferred. As was to be expected, a far greater quantity of duodenal juice was obtained in this group of cases. However, although the difference in this respect was marked between infants of one week and one month, it was slight between those of a month or two and those of five or six months. It should be borne in mind that the total secretion for twenty-four hours was never collected, as this was not practicable.²⁴

It was found that whereas infants during the first week of life secreted about 2 c.c. of duodenal fluid in the course of a test of a half hour, infants a month or two old secreted 4 to 5 c.c. On surveying the results of the tests of infants of this group, it seems as if we can make only broad quantitative deductions. Trypsin, it will be remembered, was present to a marked degree in younger infants, as was lipase, and it is only in the case of amylase that we can state that an enzyme was present in older infants in increased amount. For, whereas in the cases under group *b* the glucose formed by the amylase was never sufficient to entirely reduce the 10 c.c. of Fehling's solution used for the test, in these older infants, frequently half of the incubated fluid was able to effect this result. The most marked amylolytic action was obtained with the fluid from an eleven-weeks-old breast-fed infant, in which case 12.7 c.c., that is about a quarter, of the test fluid completely reduced the Fehling's solution. These results have a clinical bearing which will be discussed below.

It has been asserted by some,²⁵ but denied by others, that the pancreas has a selective activity; that when the food contains a great deal of fat, for example, a lipase of proportionately marked lipolytic power is secreted, and so with the other ferments. Judging from our experiments this would not seem to be the case, for a baby fed on skimmed milk had a lipase equivalent of 3.0 c.c., two fed on milk with 3 per cent. fat had a lipase titrating at 2.2 c.c. and at 2.4 c.c., and still others being fed on milk containing 2 per cent. fat had a lipase varying from 0.9 c.c. to 6 c.c. Nor could a parallelism in this respect be drawn from the results of the protein and starch content of the food, and the respective amounts of trypsin or amylase in the duodenal fluid. Indeed, if the relationship exists, we should expect the nursing infant to have no amylase whatsoever, or at least a marked deficiency compared to an infant receiving a decoction of cereal. On the contrary, the amylase of the two nursing babies was quite as active as that of infants taking milk and barley water, which, from a clinical point of view, would argue strongly against absolute specificity in the secretion of the pancreatic cells.

24. Recently we have devised a catheter which is self-retaining and with its aid we hope to be able to overcome this difficulty and to collect the secretion for long periods.

25. Pavlov, I.: *The Work of the Digestive Glands*, Ed. 2, 1910, p. 140.

2. *Pathologic Cases.*—*a. Marantic Infants (Atrophy, Decomposition).*

—It was with especial interest that we tested a number of infants suffering with severe marasmus, for a lack of intestinal ferments, the more particularly as a deficiency of pancreatic ferments has been suggested as the cause of this ailment. A few years ago Wentworth²⁶ presented the hypothesis that marasmus was due primarily to the fact that the infant received an improper food, resulting in the secretion of an inadequate gastric juice, which in turn failed to stimulate the cells of the duodenum to elaborate normal secretin. As the flow of pancreatic juice is supposed to depend for stimulation on this hormone, an insufficiency of ferments naturally results. This hypothesis was based on finding a diminished amount of secretin in the mucosa of the intestine of the atrophic, compared to the normal, infant.

Unhappily there is little difficulty in finding marantic infants in hospitals; fourteen were tested. Many were greatly wasted, most of them weighed 6 to 7 pounds, although 2 to 6 months old. It was soon evident that these infants had pancreatic juice containing enzymes of no mean activity. The lipase frequently titrated at 2 to 3 c.c., the amylase converted sufficient starch solution to completely reduce the Fehling's solution, and the trypsin digested the gelatin within twenty-four hours. This was not the exception, but rather the rule. Nor can we fall back on the assumption that the total quantity of pancreatic juice was deficient, for it was fully as copious as in the former group of cases. Indeed in marked marasmus we occasionally meet with a most interesting form of pancreatic hypersecretion, quite different from the cases associated with gastric hypersecretion which will be considered below, a form which may be termed "paralytic hypersecretion." In these cases, there is an almost continuous flow of alkaline duodenal fluid, containing all three pancreatic ferments. The following two instances are typical:

CASE 1.—W. E., 3 months old. Marasmus. Weight 6¾ pounds. Receives 2 ounces of milk every two and one-half hours containing approximately 2 per cent. fat, 6 per cent. sugar, 1 per cent. protein.

Oct. 30, 1911. Catheter passed one and one-half hours after feeding; stomach almost empty; contains a small amount of neutral fluid. Pylorus readily traversed. In three-fourths hour 12 c.c. of fluid was aspirated; in one hour 20 c.c. This fluid was obtained while the end of the catheter was about 5 cm. below the pylorus. It was yellow, viscid, alkaline. The secretion was noted as the most constant and profuse yet obtained. When the test was discontinued after one and one-half hours, the secretion seemed somewhat less marked. At this time a test of the stomach contents, which were very scanty, gave a neutral reaction. The infant died four days later. This fluid was 0.2 acid to 1/20 N. NaOH. It contained no lipase, amylase 50, and digested gelatin within twelve hours.

26. Wentworth, A.: Jour. Am. Med. Assn., July 20, 1907, p. 204.

CASE 2.—Dec. 11, 1911. J. C. 5½ months old. Weight 6¾ pounds. Fed every three hours, 4 ounces of a mixture containing 13 ounces whole milk, 11 ounces water, 1 ounce dextrin malt preparation.

Test two and one-half hours after feeding.

2:25, about 2 ounces of food evacuated from stomach; gas, foul odor.

2:30, catheter passed into duodenum.

2:40, 10 c.c. of alkaline, somewhat cloudy, yellow fluid aspirated.

2:55, 8 c.c. more fluid obtained.

3:00, 6 c.c. watery, neutral yellow fluid.

3:07, 3 c.c. slightly alkaline, faintly bile-colored fluid.

3:12, 2 c.c. darker, thicker, more alkaline fluid.

3:18, 3 c.c. neutral fluid.

3:27, 6 c.c. yellow, slightly alkaline fluid.

3:35, 2 c.c. alkaline, cloudy fluid.

3:40, 2 c.c. more fluid.

3:45, Catheter withdrawn. In seventy-five minutes 45 to 50 c.c. of duodenal fluid was aspirated. The amount of secretion in this wasted infant equaled that of the normal adult.

A previous test three days before had shown a similar but somewhat less marked secretion. At that time the fluid tested as follows: 0.3 acid to 1/20 N. NaOH, lipase 0.9 c.c., amylase 33.5 c.c., gelatin digested in twenty-four hours. The fluid obtained at the second test was 0.1 acid, gave a reaction of 0.7 c.c. to lipase, of 29.3 c.c. for amylase, and digested the gelatin in twenty-four hours.

Here are two instances of a hypersecretion of pancreatic juice in markedly marantic infants, where the normal stimulus of hydrochloric acid was absent or greatly diminished. We have termed this condition paralytic succorhea or hypersecretion because it seemed to resemble the paralytic secretion of the salivary glands which Claude Bernard²⁷ was able to incite by dividing the chorda tympani nerve. In dogs an anomaly of secretion similar to that which we have described has been observed, as the result of a diseased condition of the pancreas—continuous watery pancreatic secretion similar to a transudate.²⁸ In these animals changes denoting exhaustion were found in the glandular acini; it would be interesting to compare this condition with the microscopic picture of the pancreas in a case of "paralytic hypersecretion" in an infant.

b. Pylorospasm Associated with Gastric Hypersecretion.—We have made a separate grouping of the cases of pylorospasm because generally they are associated with an abnormality of secretion, the secretion of gastric juice. Clinically they are frequently included in the general classification of marasmus, a name used to cover a great variety of conditions. However, in most marantic infants hydrochloric acid is deficient, whereas in these cases it is increased, and we have a status which closely resembles simple starvation, brought about by an insufficient quantity of food entering the intestine. In the ordinary case of marasmus, on the contrary, enough food reaches the intestine, but is not utilized as there is some disturbance of absorption or of assimilation. So that

27. Luciani, L.: *Physiologie d. Menschen*, 1906, ii, p. 62.

28. Luciani, L.: *Physiologie d. Menschen*, 1906, ii, 75.

from a metabolic point of view the two groups of cases are quite different, although they are characterized by the same chronic atrophic condition. As might be expected, the increased secretion of hydrochloric acid stimulates an increased flow of pancreatic juice, and we find a duodenal or pancreatic succorhea. This may be termed "functional pancreatic hypersecretion." A study of the duodenal juice of seven cases of this type shows that the secretion is rarely as profuse as in paralytic hypersecretion, and that it differs from these markedly in character. It is not thin and watery, but contains an average amount of lipase and other ferments, and is exceptional merely in being profuse. In one instance it was clear that for some time a hypersecretion of gastric juice stimulated a hypersecretion of pancreatic juice; this stage was followed by one characterized by a marked diminution of gastric secretion, and "functional pancreatic hypersecretion" gave way to a succorhea of the paralytic type.

3. Chemical and Physiological Observations on the Duodenal Secretion.—In the course of the many tests in the clinic and in the laboratory, we had opportunity to make interesting observations concerning the secretion of pancreatic juice and the properties of the juice itself. It was found that the pancreatic juice generally began to be excreted a few minutes after milk was given, and that it was likewise stimulated by introducing water or a 0.5 per cent. hydrochloric acid solution into the duodenum. These methods were not frequently resorted to in order to obtain the juice as they vitiated the tests. The examinations were almost always undertaken two to three hours after feeding for earlier tests introduced the error of food contamination, and later tests were found to yield a scanty amount of fluid. The mechanical irritation of the duodenum had no effect in inducing pancreatic secretion, nor was secretion stimulated by the infants sucking the catheter or a nipple. Generally pancreatic juice and bile are excreted simultaneously, the amount of bile varying, so that the color of the fluid may be a light or a golden yellow. At times in some cases, and repeatedly in others, pancreatic juice was obtained free from bile; in one case in the course of several tests bile was obtained only once. The duodenal fluid was neutral, alkaline or acid; when acid it was not saved for examination. It is commonly stated that the reaction of the duodenum is alkaline; this, however, was not found to be the case, for the reaction depends entirely on the resultant of the interaction of the alkaline pancreatic and intestinal fluids, with the acid gastric secretion. They may neutralize each other; there is frequently an excess of acid; the reaction is rarely alkaline except in the fasting period. As has been noted in animals, the fluid increases in alkalinity as it flows. When the juice is acid it is turbid, when alkaline, or when rendered alkaline by means of NaOH, it becomes clear. It was noted also that a slight degree of acidity did not markedly inhibit the action of

lipase, but that an increase in alkalinity did retard its enzyme action. In the case of trypsin, on the contrary, a slight acid reaction of the fluid almost nullified the proteolytic activity.

CONCLUSIONS

Whatever progress this investigation is able to offer is due to the introduction of a new method. Heretofore we have had to content ourselves with a study of the pancreas after death or of the stools during life, to gain an insight into the activity of the pancreatic ferments. With the aid of the duodenal catheter, which was devised for the diagnosis and treatment of pyloric obstruction, the opportunity presents itself for the first time of making a direct test of the duodenum in infancy, a test similar to that which is employed in investigating the secretions of the stomach.

By this means fluid was aspirated from infants varying in age from a few hours to a year, some normal, some ailing and was examined for amylase, lipase and for trypsin.

A considerable number of new-born infants were tested before they had been put to the breast. It is of physiologic rather than of clinical interest to note that without the stimulus of food to incite secretion, the three pancreatic ferments were found in the intestine.

During the first week of life the amount of the pancreatic secretion is still very scanty, but it contains the starch splitting enzyme with increased regularity.

In older infants, a month or more of age, there is both an increase in the quantity of pancreatic juice, and a decided augmentation of its amylolytic power. This is a most remarkable functional activity, and one difficult of biologic explanation; for to what purpose is the starch-splitting ferment adapted at this age? It would seem as if the infant was furnished with enzymes competent to digest not only its natural food, mother's milk, but also artificial food. This amylase has the power of digesting a 1 per cent. starch solution, or, for example, barley water, and therefore bears out the old contention of Jacobi²⁹ and of Heubner³⁰ that food containing starch can be utilized by the infant in the first month of life.

It seems unwise at present to draw conclusions of an absolute quantitative nature from the tests of ferments; however, we were unable to demonstrate a selective activity of the pancreatic juice — such as an increased strength of amylase when barley water was mixed with the milk, or of lipase when the percentage of fat was increased. The secretion of a large amount of amylase by the nursing baby would also argue against absolute specificity in this regard.

29. Jacobi, A.: *Gerhardt's Handbuch*, etc., 1876, i.

30. Heubner, O.: *Berl. klin. Wchnschr.*, 1895, p. 201.

Some sick infants were tested. It was soon evident, in a study of marasmus, that the hypothesis is untenable, which suggests that this disease is associated with or is caused by a deficiency of these ferments. Even in advanced cases they were not lacking. It would seem probable, therefore, that absorption is not essentially defective, for the pancreatic enzymes are concerned mainly with the preparation of food for absorption, but that the essence of this disturbance is one of retention and assimilation.

Some of these atrophic infants, although secreting little gastric juice to act as a stimulus, secreted a very large amount of thin, watery juice, containing all the pancreatic ferments, although weak in lipase. This pathologic condition we have termed "paralytic hypersecretion or succor-rhea," as it suggested the hypersecretion following the severing of the chorda tympani nerve. The loss of alkali due to the outpouring of this secretion, which serves no end, as it does not neutralize acid, may constitute an important loss to the body, and seems worthy of further study. This is all the more probable when we consider that dogs with pancreatic fistulæ cannot be kept alive for long periods unless they are given alkali.

Cases of pylorospasm associated with gastric hypersecretion furnished numerous examples of pancreatic overactivity of a quite different nature. In these instances the gland probably was overstimulated by the normal agent, the gastric juice. Such cases may be termed "functional pancreatic hypersecretion," and later may develop into the paralytic type.

It gives me pleasure to acknowledge my indebtedness to Dr. Chapin of the Post Graduate Hospital, for the privilege accorded me of carrying out a large part of this work in his wards, and to thank Miss Eleanor Fish and Miss Gertrude Fisher for their able assistance.

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INFANTILE ECZEMA AND INDIGESTION

PRELIMINARY CLINICAL STUDY WITH ILLUSTRATIVE CASES *

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About two years ago in comparing some then recent clinical experiences, we were struck by the apparent frequency with which the eruption of infantile eczema was associated with a disturbed digestion in a series of cases. From the dermatologic point of view this association was so common as even to suggest at first thought that the digestive disturbance was always present. Reflection soon showed the fallacy of the idea, as, however frequently this double condition might be encountered by the dermatologist, the pediatricist's experience proved beyond question that there are many more children without eczema than with it, even in the presence of pronounced digestive disturbances. The conclusion is unavoidable that the digestive disturbance, even in the eczematous individual, must be regarded merely as an intermediate or contributing factor in the production of the cutaneous manifestations. This preliminary report of our investigations, which is offered for your discussion, deals then with but that small phase of the general problem of infantile eczema which concerns itself with the limited number of cases in which indigestion was actually accompanied by eczematous inflammation.

Three broad questions presented themselves for study in connection with this limited group: (1) type of eruption; (2) character of the concomitant digestive disturbances; (3) frequency with which a definite type of eruption could be demonstrated to occur in connection with a definite form of indigestion.

The first step was naturally to gather all the facts which each case showed as regarded both the cutaneous and the digestive conditions.

The second step was to scrutinize the combined records in a general way, first from a dermatologic and then from a pediatric point of view in order to determine whether the general conclusions justified a further, more detailed study of the subject.

Having decided that the cutaneous and digestive conditions were more or less definitely constant, there remained only the task of deter-

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*Read in the Section on Dermatology of the American Medical Association, at the Sixty-Third Annual Session, held at Atlantic City, June, 1912.

mining by a detailed analysis of the data whether a definite type of eruption was always associated with a definite form of indigestion.

We propose to offer the facts for your consideration in this same order, presenting first the general review from both the dermatologic and the pediatric points of view and then the detailed considerations of both.

THE ERUPTIONS — GENERAL REVIEW OF DATA

The method of obtaining clinical facts is so ordinary and familiar as to need no description. We may therefore state without further detail that the skin records seem to lead to the general conclusion that the eruptions of infantile eczema might be divided with a fair degree of definiteness into two groups. Occasionally, however, a case was seen which presented characteristics belonging to both and which might therefore be considered as intermediate. The dominant features which differentiated the eruptions of the first group (to which we will hereafter refer as Group I) from the second (Group II) were the greater acuteness and intensity of the inflammatory process and its more pronounced tendency to exudation. A more detailed account of these two eruptive types will be given further on.

THE DIGESTION — GENERAL CONSIDERATIONS

Next comes a similar preliminary analysis from the pediatric point of view.

The facts concerning the state of the digestion have been collected through the analyses of the stools which one of us (F. B. T.) has made. As this method of stool examination in connection with the study of the digestive processes in infants has been developed but recently, a brief description may be necessary to a proper appreciation of the value of conclusions based on information obtained in this manner. To the disturbances of digestion an etiologic connection with the production of eczema in infants has been attributed many times before, but the coarser methods of investigation, which alone have been available hitherto, have invariably failed, in the absence of clinical symptoms, to furnish the necessary proof.

The recent advances in our knowledge of the physiology and pathology of infant digestion, however, have thrown much light on many formerly obscure conditions. Consequently, in the diagnosis and treatment of the diseases of the infantile digestive tract, the pediatricist now considers the examination of the stools as important a routine measure as auscultation in diseases of the lungs or urinalysis in affections of the kidneys. For example, in the presence of a disease of the lungs we cannot make an accurate diagnosis from the clinical symptom of cough alone. In the indigestions of infants the clinical symptoms do not tell whether they

are due to the fats, to the carbohydrates or to the proteins. In the first instance, we can obtain by auscultation an accurate idea of the conditions in the lungs which have produced the cough. In the same way the examination of the stools yields to the pediatricist accurate information concerning the process of digestion in the infant. Through the facts gathered from many previous investigations and experiments he can interpret with fair accuracy from the results of the stool analysis whether the indigestion is due to the fats, the carbohydrates or the proteins, and can then regulate his treatment accordingly.

Two methods are used in the examination of the stools — the macroscopic and the microscopic — which supplement each other. The technic of the microscopic method and, most of all, its accurate interpretation, demand such extensive and specialized experience that we cannot at this time enter on its detailed description. The macroscopic method, however, is so much more easily learned that a brief summary of the macroscopic features presented by the stools in the different disorders of the infantile digestion may be of value in connection with this report.

Through the more intimate data collected by the microscope used in conjunction with the grosser method of macroscopic inspection, it is now possible to differentiate with greater accuracy than before the form of the indigestion by the macroscopic appearances presented by the stool.

The most common fat stool is soft and contains in varying abundance soft curds which have been found to be composed of fat in the form of fatty acids or soaps. These curds look like small particles of undigested milk imbedded in a mucus which is usually more or less greenish. The "soap stool," a second form of fat indigestion, is of a light yellow or whitish color, has a shiny surface, a soapy appearance and is almost entirely composed of fat. There is a third but less common type of stool, almost wholly composed of fatty acids, which presents the appearance of Indian meal.

An acid, burning stool is an indication that the starches, which under normal conditions are converted into sugar and in this form absorbed, have, owing to a faulty digestion, undergone a further reduction by which the sugar has been broken up into lactic, acetic or succinic acids. If an acid stool is stained with Gram's or Lugol's solution the starch granules present are stained blue.

In the case of lactalbumin and whey, protein indigestion gives no clinical signs in the stools; but the presence of tough, bean-like curds indicates that casein digestion is disturbed.

The macroscopic examination, however, does not help us to determine the relative amount of fats contained in the stool nor does it reveal the presence of small amounts of starch. This information can only be

obtained by the microchemic examination. The microscope must also be used to detect the content of meat fibers, cellulose and vegetable detritus.¹

The fundamental principles so sketchily described above were applied to the analysis of the information afforded by such macroscopic and microchemic examinations of the stools.

TYPES OF INDIGESTION IN ECZEMA

A general survey of the data seemed to indicate that there were two types of indigestion associated with infantile eczema; one, a variety of fat or carbohydrate indigestion; the second, a grosser form of which the chief evidence found in the stools was the presence of undigested particles of solid foodstuffs.

In order to determine if the conclusion, drawn from the facts relating to the question whether infantile eczema manifests itself in two eruptive forms, has any significance in view of the second conclusion, drawn from the statement that two forms of indigestion were encountered in infants with eczema, we must make a detailed analysis of the data on which these general conclusions were based. The final conclusion will be contained in the answer to the question: "Is the relationship limited to a definite form of eruption with a definite type of indigestion?" Or, to put the question in another way, "Can it be demonstrated that a given type of eruption is associated sufficiently often with a definite form of indigestion to render the conclusion probable that their association is not mere accident?" The answers to these questions must be found in the observations recorded above, testing the conclusions to which the dermatologic records would lead the student by the conclusions apparently indicated by the facts recorded by the pediatricist.

As the most graphic method of presenting the facts, we shall recite the histories of certain selected cases to illustrate the types of eruption which are usually found in association with the various forms of indigestion, as of fats, carbohydrates and the solid foodstuffs.

ERUPTIONS IN GROUP I

Therefore Case 9 is given to illustrate the type of eruption which is usually encountered in the presence of an indigestion of fats.

CASE 9.—The patient, a baby, was originally admitted to the hospital with a vesicular dermatitis which involved nearly the whole head and also a few small areas on the body. He was given a food formula which figured 4 per cent. fat, 7.7 per cent. sugar and 2 per cent. protein. An examination of the stool made seven days before discharge, i. e., one month after admission, showed an excess of fats in the form of soaps. Although this indicated that the infant was being given more fat than he could digest, the formula was not changed at this time. When discharged from the hospital the skin was seemingly about well.

1. A detailed description for those interested in the technic of the microchemic examination will be found in the Archives of Pediatrics, February, 1911, xxviii.

Three days later he was readmitted to the hospital with a recurrent vesicular eruption which this time was limited to the cheeks, forehead and chin. He was again given the same food formula as when in the hospital before of 4 per cent. fat, 7 per cent. sugar and 2 per cent. protein. The conditions in the skin improved, according to the record made on the tenth day after readmission. On the other hand, the examination of the stool, under the same date, recorded that the stool contained a large excess of fats, was pale yellow, greasy and sour.

It is interesting to note that the next record of the cutaneous condition, made five days after this stool examination which showed the increase in the excess of fats, states that the face had been growing worse.

Now, without altering the external treatment, the fat content of the food was reduced from 4 per cent. to 2 per cent. without other change than the addition of lime-water. This reduction in the amount of fat was promptly reflected in the findings from the stool analysis, for the very next day only a slight excess of fat was found.

In view of the fact that no change had been made in the external treatment, the note made five days later is especially suggestive: "The condition of the skin has improved much since the reduction of the fat in the diet."

Aside from the intolerance of fat, this case pictures well the sort of skin manifestations which have usually been found in association with a fat indigestion. The cutaneous symptoms gave evidence of an acute inflammatory process with a marked exudative tendency; that is, the eruption was of the type described in Group I. The case also illustrates the seat and the characteristic spread of this type. Attention must also be called to the suggestively significant appearance of undigested fat in the stools several days before the outbreak of the eruption.

Although such acute exudative inflammations of the skin as this were found, in the majority of instances, to be associated with an indigestion of fats, similar inflammations were occasionally seen in cases in which the dominating feature in the stools was not fatty excess, but undigested starch. As an illustration, Case 17 may be cited.

CASE 17.—The patient was a child of 18 months whose eczema was said to have existed since he was 6 weeks old. Since birth he had received at intervals, whose length and frequency apparently depended on his spells of crying, varying amounts of condensed milk, a food low in its fat content and high in its sugar. In addition to condensed milk he was now receiving from the common table such foodstuffs as pudding, a little rice or potato and bread and butter.

On October 14 the stool showed no free fat or fatty acids and only a slight amount of soaps, but did show, both macroscopically and microscopically, a large amount of starch. As to the skin, the record says that the face "was almost universally swollen and reddened and covered with vesicles ruptured and oozing and crusted and, to a lesser degree, the arms." "Itching was intense."

Although the mother was given definite directions concerning the diet they were only partially carried out. Still, even this partial modification of the diet was followed by an improvement in the cutaneous disturbances and, in the stools, by the total disappearance of the slight excess of soaps previously noted and by the reduction of the amount of starch from large to slight.

In connection with the inflammation of the skin it was noticeable that the "improvement" recorded consisted not in the disappearance of the eruption, but in the modification of its intensity. Whereas the skin manifestations were formerly of a moderately acute, exudative type, the intensity of the inflammatory

process was now greatly lessened. The eruption no longer showed exudative lesions but dry, infiltrated, profusely scaling areas situated on the body. The itching, which was once so intense as to interfere with sleep, also decreased and was no longer troublesome.

From the dermatologic point of view the interesting feature in this case is the behavior of the eruption. With the indigestion of fat present, the cutaneous symptoms were those of Group I which, coincidently with the elimination of the fat indigestion, declined to the type of Group II notwithstanding the persistence of a small amount of starch in the stools.

From the pediatric point of view attention is attracted to the disappearance of the clinical symptoms of indigestion which followed the reduction of the amount of starch in the food and to the gain in weight and improvement in the general appearance of the patient.

Case 31 was exceedingly interesting because of the seemingly close connection between the disturbances in the skin and the disturbances of the digestion. So parallel were the fluctuations of the eruption to the changes in the digestion that the suggestion of their relationship was unavoidable.

CASE 31.—When first seen the child was 5 months old and showed no particular disturbance of the skin. He was undersized and was reported to have a poor digestion and to have gained nothing in weight in the last three weeks. His food formula showed that he had been receiving 5 per cent. of fat, 6 per cent. sugar and 1.5 per cent. protein. There were present symptoms indicative of a chronic intestinal indigestion due to fat. The formula was accordingly changed to fat 2 per cent., sugar 7 per cent. and protein 1.65 per cent.

This increase in the amount of sugar from 6 per cent. to 7 per cent. was followed immediately by marked symptoms of sugar indigestion and two or three days later by an eruption on the skin.

A reduction of the percentage of sugar from 7 per cent. to 5 per cent. gave relief from the symptoms of the indigestion of sugar. The fat indigestion was not affected. The digestive balance, however, was now so delicate that slight changes in the formula sufficed to induce a return of the clinical symptoms of indigestion.

Coincidentally with the appearance of the symptoms of sugar digestion which followed the increase in the percentage of sugar in the diet, the skin showed disturbances due to an acute, exudative, inflammatory process which were extensively distributed over the body, extremities and head, but which it must be noted were equally as intense on the body as on the head, although the eruption was everywhere exudative.

The intensity of the cutaneous manifestations declined as the conditions due to the indigestion of sugar improved but nevertheless persisted, as did the indigestion of fat. Thereafter, however, the cutaneous reactions were so sensitive that the slightest dietary indiscretion was followed almost immediately by an increase in the intensity of the symptoms in the skin. The interest in this lies in the coincident increase in the delicacy of the digestive balance, already mentioned.

ERUPTIONS IN GROUP II

Contrasted with these acute inflammatory disturbances of the skin in which the exudative tendency was a prominent feature and in which the associated digestive disturbance was usually due to fat, were the

eruptions in which the picture in the stools of an indigestion of fats and starches was subordinate to the symptoms of an indigestion due to more solid foodstuffs. These digestive disturbances of Group II were usually accompanied by a cutaneous eruption of moderate or mild intensity which lacked the tendency to exudation described above (Group I) and, in several other particulars which will be referred to again, differed from the symptoms of the cases in Group I. Nevertheless, we can advance no proofs as to the etiology of Group II as the changes in the digestive processes do not manifest themselves in the stools in any definite manner. For the present, then, we must abandon the cases in this group, leaving to the future the discussion of such questions as the meaning of the greater intensity of the skin reaction when associated with fat intolerance.

Scrutinizing the facts summarized above, the impression given is that whereas the exudative inflammatory processes for the relief of which the patient sought the dermatologic clinic showed a constant, though perhaps not absolute, association with the disturbances of digestion due to fat and occasionally to the carbohydrates, but rarely to any other forms of indigestion; the non-exudative cases of Group II were rarely associated with the dominance of the stool picture by fats. Oftentimes, indeed, the stools contained neither fats nor carbohydrates in abnormal amounts. In other words, the indigestion of fats and carbohydrates was an exceedingly frequent accompaniment of the exudative inflammations of the skin in contrast to the results of the stool examinations in the cases of Group II.

NATURE OF EXUDATIVE ERUPTION

These indications obviously pointed to a more careful study of the acute, exudative inflammatory process as the next step. Briefly stated, the following were the important facts revealed:

The general aspect and composition of the eruption were the same as that which we commonly associate with vesicular eczema and was therefore not characteristic.

The course of the inflammatory process and the evolution of the lesions also corresponded to the familiar course and evolution of vesicular eczema.

The prodromal symptom of pruritus preceded the eruption by an interval the length of which varied within wide limits in the different individuals.

The onset of the eruption varied from acute to moderately acute.

The primary seat was, almost without exception, on some portion of the head, ordinarily the cheeks, less frequently on the forehead or scalp and occasionally on two or more of these regions nearly, if not quite, simultaneously.

It was the tendency of the exudative eruption to remain limited to the regions of the head for an appreciable length of time, even for months. Many cases, in fact, showed no tendency to spread to other parts.

When the eruption did appear elsewhere than on the head, its spread was from above downward, invading one part after another in orderly succession.

However great and extensive the spread, the most intense manifestations always appeared on the cheeks and, in a slightly lesser degree, on the forehead and scalp.

The eruptions which appeared on other regions than those of the head were most often encountered on the lower portions of the abdomen, the sides of the chest and on the buttocks, all of which regions are notably exposed to external traumas. The chin was affected in less than 10 per cent. of the cases and the upper and lower extremities even less frequently.

The eruption on the face was symmetrically distributed. The lesions were usually abundant and discrete for a variable length of time, but eventually coalescing over the flush areas of the cheeks, where they were always in the greatest abundance, to form oval placards of considerable size. The cheeks not covered by the large patches bore discrete lesions whose numbers decreased as the distance from the main seat increased. Even in the most severe cases a zone of skin free from all eruptive manifestations completely surrounded the lesions on the cheeks.

The eruption appeared occasionally on the auricles of the ears, but never by direct extension of the process from the cheeks.

On the forehead, the inflammatory process, when fully developed, manifested itself in the form of a broader or narrower band which occupied the middle portion of the forehead. The process never extended quite to the hair line or to the brows, and rarely appeared between the brows.

The eruption on the scalp was usually not abundant but consisted of a few scattered, roundish patches which were most often seated on the lower parts of the sides of the head.

The eruption on the scalp was usually not abundant but consisted of eczema recently described so comprehensively by Brocq. It occurred there in round, moderately well-defined patches, in moderate abundance. In an occasional case the patches were present in greater numbers and, by confluence, even covered considerable areas.

The form of eruption was the same on the lower abdomen and the extremities as on the chest except that, on the abdomen, it showed a greater tendency to confluence and, on the wrists, a greater intensity, as was manifest by the more numerous papulovesicles, their brighter color and sharper definition.

Itching was a usual accompaniment of the eruption, but was less intense in most "acute" cases than in the subacute or subchronic cases of Group II. The fact was noteworthy that, as the eruption improved, the itching and the feeling of irritation increased.

The cutaneous reaction was increased over the body surface generally regardless of the presence or absence of eruptive manifestations.

The course of the cutaneous symptoms was marked by the same irregular fluctuations in intensity as are met with in ordinary eczema.

IRREGULARITY OF NON-EXUDATIVE ERUPTIONS

If the symptoms of the subacute or subchronic eruptions of Group II are compared with the eruptions of Group I, just described, it will readily be seen that in no particular do they exhibit the same constancy or regularity.

In general aspect, the eruption resembled that of a papular or a papulovesicular eczema of mild intensity with little tendency to exudation.

The course, although fluctuating, exhibited less pronounced changes.

The prodromes and the onset were much the same as in the acuter type.

The primary seat of the eruption was not at all constant. Except that the eruption usually made its first appearance on some part of the trunk or extremities, nothing characteristic was discovered.

The eruption was not infrequently unilateral and limited to a single part.

The character of the spread was irregular and disorderly.

The general cutaneous irritability was less disturbed.

The eruption usually manifested itself in the form of more or less abundant patches, irregularly and often unilaterally distributed and varying greatly in size. They were ill-defined, but slightly infiltrated, pale red, exfoliating abundantly and covered by a larger or smaller number of pale red, fine, acuminate papules. In the immediate neighborhood, widely separated, discrete papules were to be seen. Occasionally a few papules showed small vesicles on their summits. Occasionally also one or two patches were distinguished by a more marked tendency to exudation than their fellows and developed a considerable number of discrete papulovesicles. Such appearances, however, were not characteristic of this type and were but transitory and occasional conditions.

SUMMARY

Definite conclusions are, of course, not possible from this incomplete study of the etiologic relationship of indigestion to infantile eczema. Tentative conclusions may perhaps be allowed. In such fashion it is suggested that:

1. The acutely inflammatory form of eruption in infantile eczema presents so many features which are constant in occurrence and in form that its claim for consideration as a definite, fixed type of disease deserves further attention.

2. For directly opposite reasons, the less intense inflammatory form of eruption cannot lay claim to such consideration.

3. The stool findings show that the indigestion of fats and of carbohydrates are the only types which can be demonstrated to occur with any regularity and definiteness in association with infantile eczema.

4. The occurrence of the acute exudate type of eczematous inflammation of the skin in such frequent association with an indigestion of fats and sugar indicates that the process in the skin and the process in the digestive tract probably have some etiologic relationship.

5. Contrariwise, the fact noted at the outset that the majority of infants presenting the same symptoms of indigestion described above do not likewise present a cutaneous reaction points to the inevitable conclusion that some underlying condition, probably systemic, which the eczematous infants possess, is lacking in the non-eczematous individuals.

6. Therefore, indigestion must occupy an intermediate position, if any, in the mechanism of the production of eczema.

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INTESTINAL TOXEMIA IN THE NEW-BORN *

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The condition of which I shall speak as intestinal toxemia of the new-born is, I am inclined to think, not at all an uncommon one. All who have much to do with the new-born infant must be more or less familiar with it. The text-books, however, either do not refer to it at all or so casually that the reference is very likely to be overlooked. This is probably because the writers have considered it too simple a matter to describe or because they have described it under other names or in connection with other diseases. The majority of the cases of what I have considered to be examples of this condition which I have seen in consultation have, however, been mistaken for other diseases.

I shall base my description of the symptomatology of this condition on the cases which have recovered, as none of the babies which have died of what I have supposed to be intestinal toxemia have been autopsied.

SYMPTOMATOLOGY

A baby that was normal at birth and has continued to seem normal and to do well up to the second, third, fourth or even fifth day, becomes rather suddenly ill. He is likely to cry and moan considerably, although he is not infrequently unusually quiet. Attacks of cyanosis are a common and early symptom. Twitching of the extremities, slight general rigidity and retraction of the head come on in many instances, while convulsions are not infrequent. The temperature is, as a rule, only moderately raised, but may be high. In the more severe cases the baby refuses to nurse. Vomiting is uncommon. There is in most instances no diarrhea; in fact, the tendency is to constipation. In the majority of instances the symptoms develop before the baby has ceased to pass meconium and it is very common to find that it has not passed as much as the average baby. If the stools are not composed of meconium, they are usually small in amount, loose, dark-brown and contain small, soft curds and mucus. They are often offensive. The abdomen may be distended, but usually is not. Loss of weight is generally rapid, the face becomes pinched and in all but the mildest cases it is evident that the baby is seriously ill. If the

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bowels are thoroughly cleaned out, all food stopped for a time and water given freely, recovery is usually rapid and complete. If the bowels are not cleaned out and food is continued, a fatal termination is not uncommon and recovery is, in any event, slow.

CASE REPORTS

The following case histories illustrate the symptomatology of the condition:

CASE 1.—Henry H. was born at 1 a. m., January 25, after an easy, low forceps delivery. He was normal at birth and weighed 8¾ pounds. He passed both urine and meconium immediately after birth. He was put to the breast at the ordinary intervals after twelve hours, but apparently obtained very little. He seemed all right, except that he cried considerably, until the morning of January 26, when he became very fussy and his temperature was found to be 102 F. The bowels moved during the afternoon, the movements consisting of meconium. He was given two feedings of 1 ounce each of a mixture containing 1.50 per cent. of fat, 4 per cent. of milk sugar, 0.25 per cent. of casein and 0.25 per cent. of whey proteins. He became a little quieter after this, but his temperature at 6 p. m. was 103.5 F. He was seen in consultation at 9 p. m., January 26.

He was well developed and nourished and of good color. Nothing whatever abnormal was found on a careful physical examination. A movement, which was seen, consisted entirely of meconium.

He was given a teaspoonful of castor oil, all food was stopped and water was given freely. The bowels moved several times during the night and the temperature the next morning was 99.5 F. He was then fed again, partly on the breast and partly on the bottle, but there was no recurrence of the symptoms.

CASE 2.—Helen P. was born at 12 m., July 17, after a moderately severe labor induced two weeks ahead of time because of albuminuria in the mother. She was the second of twins. She weighed 6¾ pounds. She was pale, but cried fairly vigorously. She was quiet during the afternoon, but in the evening began to cry and moan. She had kept this up almost continuously. Usually there was a moan with each breath, but at times she cried hard, as if in pain. She passed urine freely, but did not pass any meconium until the early afternoon of July 18. She had had no food, but had taken a little water. She was seen at 5:30 p. m., July 18.

She was fairly developed and nourished and of good color. The fontanelle was somewhat depressed. The pupils were equal and reacted to light. The mouth and throat showed nothing abnormal. She was able to swallow. The heart and lungs were normal. The abdomen was somewhat distended, but otherwise normal. The lower border of the liver was palpable 3 cm. below the costal border in the nipple line. The spleen was not palpable. The navel was healthy. The extremities were normal. There was no spasm or paralysis. The knee-jerks were equal and normal. There was no Kernig's sign. She moaned with each inspiration and acted as if in pain. The rectal temperature was 100.4 F.; the pulse, 160; the respiration 68.

She was given a suds enema and a teaspoonful of castor oil at once. Water was ordered to be given freely during the night and a weak modified milk the next morning.

Considerable meconium was obtained with the enema and the bowels moved freely during the night. The temperature was normal the next morning and she was perfectly comfortable. She did uninterruptedly well from that time on.

CASE 3.—Granville W. was born October 12, after a very rapid labor, two weeks ahead of time. He was normal at birth and weighed 6 pounds. The breast milk came in on the third day and he took it fairly well.

He had been given special care, but had been dressed and bathed. He seemed to be doing well until the morning of the third day, when he had an attack of cyanosis lasting a minute or two. The pulse went up to 180 during the attack, then dropped to 120. He had several similar attacks during the morning, and at noon the attacks of cyanosis were accompanied by irregular contractions of the face and hands. The head and eyes were always turned to the right. He was given paregoric and bromid and had no attacks for twenty-six hours. They recurred, however, on the morning of the fifth day. The twitching was then most marked in the left side of the face and in the left hand. The temperature had not been above 99.2 F. He was partially cleaned out with sweet oil and magnesia in the beginning. The bowels had not moved very well since then. He had not vomited. He was seen at 4 p. m., October 18.

He was small and thin, but of good color. He opened his eyes, looked about, gaped and acted like a normal baby. The fontanelle was slightly depressed. There was no rigidity of the head or neck. The pupils were equal and reacted to light. There was no spasm or paralysis of any of the muscles controlled by the cranial nerves. The heart, lungs and abdomen were normal. The liver was palpable 2 cm. below the costal border. The spleen was not palpable. The stump of the cord and navel were healthy. There was no spasm or paralysis of the extremities. The knee-jerks were equal and normal, the abdominal and cremasteric reflexes lively. Kernig's sign was absent. The last movement, which was seen, was watery, dark-brown in color, contained many fine curds and was foul in odor.

He was given a teaspoonful of castor oil, the breast milk was stopped and whey, $\frac{1}{2}$ to 1 ounce, every two hours, ordered. After the bowels were cleaned out he had no recurrence of his symptoms and did uninterruptedly well.

CASE 4.—John H. was born at full term, after a normal labor, October 28. He seemed normal at birth and weighed $9\frac{1}{4}$ pounds. He was put to the breast and took it well. He seemed a little feverish October 30, but the temperature was not taken. The next day he was dusky, and the temperature was found to be 103 F. He breathed with some difficulty, as if there was some obstruction, had clonic motions of the face and rolled his eyes. The temperature from this time on ranged between 103.6 F. and 104.8 F. He had much difficulty in nursing and swallowing, but did not vomit. The movements continued to look like meconium. He began to hold his head backward November 2. He was seen in consultation at 5 p. m., November 2.

He had evidently lost much weight. His face was pinched and he seemed very feeble. The fontanelle was depressed. He was generally somewhat dusky. The lips and skin were dry. The heart, lungs and abdomen were normal. The navel was healthy. The liver was palpable 3 cm. below the costal border in the nipple line. The spleen was not palpable. There was no spasm or paralysis of the extremities. The knee-jerks were equal and normal. Kernig's sign was absent. The pupils were equal and reacted to light. There was no dulness under the manubrium and no tumor was felt in the suprasternal notch. The rectal temperature was 103.8 F.; the pulse, 160; the respiration, 45. The movements which were seen were small, dark-green, sticky and contained a few fine curds.

He was given a teaspoonful of castor oil and diluted breast milk and whiskey. The bowels moved freely, the temperature quickly came down to normal and he made an uninterrupted recovery.

My interpretation of the etiology of these cases is that a bacterial infection of the meconium, through either the mouth or anus, takes place within the first twenty-four or forty-eight hours after birth; that on account of the incomplete evacuation of the intestines the toxic products

formed in the meconium as the result of this infection are absorbed into the circulation and that these toxic products cause the symptoms. Corroborative evidence in favor of this conception is that, as the meconium is made up of protein, the products of bacterial action in it must necessarily be putrefactive in character and, therefore, toxic. It is a well known fact, moreover, that cyanosis may be enterogenous in origin. It may be asked why this symptom-complex is not merely a manifestation of septic infection, that is, of the entrance of bacteria into the circulation. I am unable to say positively that this is not the case, because no blood cultures were made from these patients. The early onset of the symptoms, the absence of any nidus of infection and the absence of other signs of sepsis, such as hemorrhages, marked jaundice and boils, make it improbable, while the rapid and complete recovery after the evacuation of the bowels seems sufficient to exclude it. It may also be asked why it is not simply a manifestation of starvation, analogous to the so-called "inanition fever." The answer is that it occurs both in babies that have not been fed and in those that have been, and that the withdrawal of food in connection with the evacuation of the bowels relieves it.

DIAGNOSIS

The diseases for which this condition is most likely to be mistaken are cerebral hemorrhage as the result of injury at birth, meningitis, hemorrhagic disease of the new-born and septic infection of the new-born. The diagnosis from septic infection of the new-born is the most difficult. The symptoms appear earlier, as a rule, than do those of septic infection and the temperature is usually lower than in sepsis. There is no local nidus of infection, and marked general and local symptoms of infection, such as hemorrhages, deep jaundice and furuncles, are absent. There is a tendency to constipation and the stools are usually meconium-like in character. In many instances it is, however, impossible to make a positive diagnosis without the therapeutic test of free catharsis. Hemorrhagic disease of the new-born can be excluded on the absence of hemorrhages. Meningitis is extremely rare at this age and, when it occurs, it is a part of a general septic infection. There is almost invariably bulging of the anterior fontanelle in meningitis and usually when there is a cerebral hemorrhage. There are usually symptoms of focal irritation in hemorrhage and often blood in the nose and nasopharynx, while in both cerebral hemorrhage and meningitis there is likely to be spasm of the extremities and exaggeration of the knee-jerks. These latter symptoms, as well as other symptoms of cerebral irritation, may, however, also be present in intestinal toxemia. A lumbar puncture will settle the diagnosis at once in a doubtful case.

TREATMENT

The treatment consists in the administration of one or two teaspoonfuls of castor oil, the withdrawal of food for from twelve to twenty-four hours and the feeding of water or water sweetened with saccharin. It is also well to irrigate the bowels in the beginning. Bromid or stimulants, such as strychnin or caffein, may be used, if necessary. The best food, after the period of starvation, is human milk, plain or diluted, according to the individual baby's condition. Next to this, a mixture of cows' milk, low in fat, high in milk sugar and with a moderate amount of proteins, part of these preferably in the form of the whey proteins. It is important to give a high percentage of milk sugar in order to change the bacterial activity from the proteolytic to the fermentative type.

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STUDIES IN METABOLISM OF AMAUROTIC FAMILY IDIOCY *

HENRY HEIMAN, M.D., SAMUEL BOOKMAN, PH.D., AND
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NEW YORK

PART I.—BY HENRY HEIMAN, M.D.

Carefully as this disease has been observed for over a quarter of a century, the obscurity regarding its true nature is still as great as ever. While Sachs¹ somewhat modified view of its congenital origin has gained many adherents, among these such careful observers as Schaeffer² and Vogt,³ there are a considerable number of authorities who hold the opinion that this affection is acquired in nature. Though few now share the view of Hirsch⁴ that some toxic substance plays a rôle in the etiology of the disease, it is on theoretical grounds alone that it has been discarded. Yet this view is not so wholly improbable or unreasonable as not to demand better founded reasons for its final abandonment. Moreover, within recent years certain observations have been recorded which seem to indicate that other organs besides the nervous system are affected in this disease. Thus Brooks⁵ has found morbid changes in the pancreas, hypophysis, thymus and adrenals. If toxic agents are at work, and more especially if the organs playing an important rôle in the production of internal secretions are affected, we may expect that the metabolic processes would show some departure from the normal.

In view of the fact that this disease is so prominently characterized by a marked and generalized degeneration of nerve cells and nerve tissue, as proved by the very thorough recent histologic and pathologic studies of Schaeffer, Vogt, Brooks, Sachs and Strauss,⁶ and others, it would be interesting to discover in the excretions the chemical evidences of the degenerative process which we know is going on. This should be evidenced by some disturbance in the excretion of those elements which are so

*Read at the Meeting of the American Pediatric Society, Hot Springs, Va., May 29, 1912.

1. Sachs: Jour. Nerv. and Ment. Dis., 1887.
2. Schaeffer: Jahrb. f. Psychol. u. Neurol., 1907, p. 121; Ztschr. d. Jugend. Schwach., No. 2, p. 75; *ibid* No. 3, p. 19.
3. Vogt: Archiv. f. Kinderh., 1909, li.
4. Hirsch: Jour. Nerv. and Ment. Dis., 1898, p. 538.
5. Brooks: Tr. Assn. Am. Phys., 1911.
6. Sachs and Strauss: Jour. Exper. Med., 1910, xii, 685.

integral a part of nerve tissue, namely, phosphorus and sulphur. Despite the valuable information that could be expected from a chemical study, this aspect of the disease has been, up to the present, almost entirely neglected. A perusal of the recent literature fails to show any extended metabolic studies. The only investigation dealing with the chemical side of amaurotic family idiocy is that of Mott. In a paper detailing the chemical analysis of the brain in two cases of amaurotic family idiocy, Mott⁷ shows a very distinct change in the relative proportions of simple and nucleoproteins, the latter being diminished, and being replaced by proteins of a simpler composition with an increased water content.

The opportunity having presented itself of observing two cases of this disease, it seemed worth while to undertake the study of its metabolism. As will be seen from the hospital records, both were typical cases of amaurotic family idiocy. The first case was submitted to one period of investigation, the second to two at an interval of twenty-four days.

CASE REPORTS

CASE 1.—The first case, David F., 15 months old, born in the United States, of Russian Jewish parentage, was admitted to the children's service of Dr. Koplik at the Mount Sinai Hospital, April 7, 1911. One other child was well.

Past History.—Full term, breast-fed for twelve months; enterocolitis of two months' duration at 6 months of age; measles at 12 months of age; never sat up nor stood up, nor made any attempt to speak; no history of convulsions. Since the attack of measles three months prior to this report, mother noted gradually increasing drowsiness and weakness. There was no vomiting, no fever, no other disturbances, but marked sweating especially at night. Bowels markedly constipated.

Physical Examination.—General condition fair, well nourished; no rigidity of neck; eyes staring, apparently blind; right pupil larger than left; pupils react sluggishly; heart, lungs, and abdomen negative; spasticity of all four extremities; reflexes not obtained.

April 28, 1911. Fundi show cherry-red colored spot in the center of a white area outside of each disk, which is atrophic and white.

Urine negative.

During the stay in the hospital, the condition of the patient did not change.

CASE 2.—The second case, H. Sch., aged 7 months, born in the United States, of Russian Jewish parentage, was admitted to the hospital Sept. 12, 1911. Family history negative. Four other children well; no miscarriages.

Past History.—Breast-fed up to time of examination. At 14 weeks of age the child had an attack of bronchitis for nine days. Mother dates illness from that time. No other diseases.

Present History.—Since attack three months prior to this report, the mother had noticed that child no longer played, but slept most of the time. Does not take the breast as readily, does not sit up, and can not stand. Child apparently can not hear or see as well as it should. No convulsions; no vomiting. Bowels move twice daily.

Physical Examination.—General condition good; patient well nourished; slightly anemic. Internal strabismus; eyes apparently follow light. Hearing normal. Loud blowing systolic at apex, heard with greatest intensity in third

7. Mott: Arch. Neurol., Path. Lab., London County Asylum, iii, 218.

and fourth interspaces. Lungs negative. Liver palpable two fingers below rib border. Spleen negative. Spasticity of both upper and lower extremities; knee-jerks normal; no ankle clonus. Cherry-red spot present. Noguchi test negative. Urine negative.

Most important in a consideration of the metabolism of such a condition as amaurotic family idiocy is the stage of the disease and the general condition of nutrition of the patient under investigation. The two children studied by us were both in an early period of this insidious malady; their general nutrition was good, muscular tissue still very well preserved, and an abundant panniculus adiposus present. So good was the general health of the children, that during the periods of observation in both cases a gain of weight was noted. Thus the patient, David F., gained 180 gm.; Patient 1, H. Sch., gained in the four days of the first investigation 80 gm.; in the second period, 30 gm. In all these instances the nourishment was well taken, the diet consisting of milk undiluted in Case 1, and diluted in Case 2. The caloric intake was in excess of the established figures of Heubner (100 calories per kilo per day).

TABLE 1.—INVESTIGATION DURING A FOUR-DAYS PERIOD OF THE DAILY NOURISHMENT OF DAVID F. (CASE 1), AGED 15 MONTHS

	Ounces	Calories
Milk	27	560
Cocoa	9	200
Broth	5	10
		<hr/> 770

Weight 8.4 kilos equals 95 calories per kilo per day.

TABLE 2.—DAILY NOURISHMENT OF SCH. (CASE 2), AGED 7 MONTHS

	Ounces	Calories
Milk	36	730
Maltose	1½	180
		<hr/> 910

Weight 7.65 kilos equals 119.3 calories per kilo per day.

The minute details of this metabolic study will be given in the second part of this paper by Drs. Bookman and Crohn. The general results of the present investigation are shown in the accompanying tables:

TABLE 3.—METABOLISM STUDY; INTAKE, OUTPUT AND DAILY AVERAGES IN AUTHORS' CASES

	INTAKE			
	N	S	P	Cl
David F.	5.831	0.5087	0.6997	1.529
Sch. (I)	3.220	0.521	0.393	0.753
Sch. (II)	5.610	1.084	1.115	1.253
	URINE			
David F.	2.834	0.23235	0.3553	0.581
Sch. (I)	1.2382	0.1075	0.121	0.3115
Sch. (II)	3.078	0.302	0.255	0.862

	STOOL			
	N	S	P	Cl
David F.	0.225	0.0775	0.0496
Sch. (I)	0.2385	0.0424	0.0104
Sch. (II)	0.076	0.084	0.1924
	TOTAL OUTPUT			
	N	S	P	Cl
David F.	3.059	0.3099	0.4040	0.581
Sch. (I)	1.4767	0.1499	0.1313	0.3115
Sch. (II)	3.154	0.388	0.4482	0.862

TABLE 4.—METABOLISM STUDY IN AUTHORS' CASES. DAILY AVERAGES

	RETENTION (PER CENT. OF INTAKE)							
	N	N %	S	S %	P	P %	Cl	Cl %
David F.	2.772	47.5	0.1989	39.1	0.2951	42.2	0.948	62.0
Sch. (I)	1.744	54.15	0.371	71.2	0.262	66.6	0.441	58.6
Sch. (II)	2.456	43.9	0.6985	64.4	0.6665	60.0	0.391	31.0
	ABSORPTION (PER CENT. OF INTAKE)							
	N	N %	S	S %	P	P %	Cl	Cl %
David F.	5.6055	96.0	0.431	84.8	0.6505	93.0
Sch. (I)	2.9815	92.5	0.4786	91.7	0.3826	97.6
Sch. (II)	5.534	98.6	1.000	92.2	0.9222	82.8

From a perusal of the data before us, we are struck by the fact that absorption from the gastro-intestinal tract and retention within the body are normal, or even better than normal, for all the constituents determined. Thus, David F. absorbed 97 per cent. of nitrogen, the normal being 88 to 96 per cent.; retention 50 per cent., the normal being 30 per cent. at this age.

Close scrutiny of the figures for the intake and output of phosphorus and sulphur does not disclose a marked disturbance in the metabolism of these constituents. As has been before stated, absorption and retention are unusually good and increased beyond normal, probably indicating a hypernormal anabolic function occurring at this stage of the disease. However, when one takes into consideration the very slow process of degeneration, extending over a period of months or years, and the very small amount of actual phosphorus and sulphur in the entire cerebro-spinal system, one can understand why, with our present methods, an abnormal elimination of these constituents would fail to be manifested in a study of this disease for short periods. It would be advisable, therefore, to study the disease at intervals during its course, both in its earlier stages in which anabolic changes apparently predominate, and in its later stages in which degenerative and catabolic processes play the important rôle.

PART II.—BY SAMUEL BOOKMAN, PH.D., AND BURRILL B. CROHN, M.D.⁸

This rather rare disease, first identified and studied by Tay and Sachs, has been subjected during the last few years to most searching investigations in regard to its clinical, pathological and histological aspects. The numerous publications throughout the literature are most complete along

these lines; we fail, however, to find any work dealing with the closer examination of the metabolic changes, if any, which accompany the morbid processes which characterize the malady in question. It occurred to us, therefore, to investigate whether the very marked pathological changes which have been repeatedly demonstrated, viz., the universal and generalized degeneration of the neurons, involving all the nerve cells, including the ganglion cells, both central and sympathetic, might not find its concomitant in some abnormal chemical variations.

With this end in view, two cases, D. F. and H. Sch., were subjected to complete metabolism studies. In each instance the patient was put onto a Heubner metabolism bed for four days. The diet was made up into exact duplicates, one of which was fed to the child, the second utilized for analysis. Urine and stool were separated by collecting the stool on a sieve, the urine being allowed to percolate through into another receptacle, and estimated every six hours, being then put on ice to prevent decomposition. The whole stool was collected for each period, sampled and analyzed. The analytical methods employed were as follows:

ANALYTICAL METHODS

Total nitrogen, Kjeldahl method.

Total phosphorus and total sulphur by fusion with sodium hydrate and nitrate.

Chlorin, incineration with sodium, carbonate and nitrate, and titration with silver nitrate. In the urine preformed sulphates in acetic acid solution, and barium chlorid, ethereal sulphate in the filtrate by further boiling with hydrochloric acid.

Total sulphates were determined by direct precipitation in hydrochloric acid solution by barium chlorid.

Neutral sulphur was estimated by difference between total sulphur and total sulphates.

Total phosphates in the urine by titration with uranium acetate (Neubauer's method).

Ammonia by the Folin aeration method.

Total acidity of the urine by titration with N/10 ammonium hydrate, using phenolphthalein as an indicator.

The stool was dried in the water-bath, after addition of alcohol and hydrochloric acid (chlorin in stool not estimated).

CASE 1.—D. F.,^{*} male, aged 15 months. One period of four days. Weight at beginning of period 8.12 kg.; weight at end of period, 8.3 kg.; diet, 48 ounces of whole milk per day; calories, 120 per kilogram. Slight but negligible vomiting occurred. (See Table 5.)

8. From the Laboratory of Physiological Chemistry, Pathological Department, Mt. Sinai Hospital.

The cases on which this study is based, were assigned from the service of Dr. Henry Koplik, attending physician, and Dr. Henry Heiman, associate attending physician to the children's service of Mt. Sinai Hospital. We wish to express our thanks to Drs. Koplik and Heiman for kind cooperation throughout the work in the wards; also to Dr. Theodore Kuttner for valuable assistance in chemical analyses.

9. For the full clinical data of the cases studied, see paper by Heiman, Bookman and Crohn, published in the Transactions of the American Pediatric Society for 1912.

CASE 2.—(Sch.⁹) This patient was subjected to two studies of four days each, with an interval of three weeks between the two periods.

Period I. Age 7½ months; weight at beginning of period, 7.39 kg.; weight at end of period, 7.47 kg.; diet 121 calories per kilogram. (See Table 1.)

Period II. Age 8¼ months; weight at beginning of period, 7.53 kg.; weight at end of period, 7.56 kg. (See Table 6.)

For a more comprehensive comparison of the above tables, we have seen fit to rearrange these in terms of daily average figures (Table 8).

Further, more carefully to analyze the individual factors entering into this metabolism study, we offer the tables and the conclusions derived therefrom (Table 9).

NITROGEN METABOLISM

Case 2 (Sch.) may be compared to the results of Rubner and Heubner¹⁰ in the study of a normal child of the same age. The retention of nitrogen in our case is markedly increased. The absorption is slightly higher in our case than in the one of Rubner and Heubner, although not exceeding normal variations (Table 10).

Case 1 may be compared to Child B of Camerer¹¹ of approximately the same age and in good health. The retention of nitrogen in our Case 2 on an intake of 5.8 gm. was 47.5 per cent., absorption 96 per cent. In Camerer's case, however, the retention was only 6 per cent. In both of our cases, therefore, absorption and retention are considerably increased. By comparison with Cronheim and Meyer's¹² figures, these deductions are further substantiated (Table 11).

CHLORIN METABOLISM

In the absence of figures for normal children of this age on similar diet, it is impossible to do more than note the high chlorin retention in our cases (Table 12). L. F. Meyer¹³ averages several previously published analyses of healthy children on mother's milk and shows but 42 per cent. retained chlorin on an intake of only 20 to 40 per cent. of that of our cases. This emphasizes the fact that the retention in our cases of 31 per cent. to 62 per cent. is remarkably high (Table 13).

PHOSPHORUS METABOLISM

The phosphorus metabolism also is noticeable for its high retention as evidenced by the figures in Table 14. Unfortunately, Keller's¹⁴ figures

10. Rubner and Heubner: *Ztschr. f. Biol.*, 1899, No. 38, p. 315.

11. Camerer: *Stoffwechsel des Kindes*.

12. Cronheim and Meyer: *Biochem. Ztschr.*, 1908, ix, 80; *Ztschr. f. Biol.*, No. 27, p. 153.

13. L. F. Meyer: *Monatschr. f. Kinderh.*, vii, 104; *Ergebn. der inn. Med. u. Kinderh.*, i, 317.

14. Keller: *Ztschr. f. klin. Med.*, 1898-99, No. 36.

in an article devoted to studies on phosphorus metabolism are not strictly comparable, for the reason that the children he studied were suffering from gastro-intestinal disturbances; neither was the intake noted, nor the excretion of phosphorus in the stool estimated.

A more recent paper by Cronheim and Meyer¹² gives figures for a normal child of about the same age as those investigated by ourselves. The absorption and retention in our cases are even higher than the results obtained by these authors (Table 15).

Keller, as well as Cronheim and Meyer and Rubner and Heubner,¹⁰ have embodied a table of ratios of $P_2O_5:N$, in their papers. Our figures based on a similar intake of nitrogen show a reduced $P_2O_5:N$ ratio in the urine (Tables 16 and 17).

SULPHUR METABOLISM

The literature contains but little of value on sulphur metabolism in children of this age; proper comparisons of only the output of sulphur can be made by utilizing the figures reported by Freund;¹⁵ these findings, however, were obtained from the study of children suffering from gastro-intestinal disturbances (Table 18).

The absorption and retention of sulphur are both apparently very high, but as no literature exists bearing on this point, we can obviously make no comparisons as regards these results.

In Case D. F., neutral sulphur and ethereal sulphates were lower than the findings in Freund's¹⁵ and Amberg and Morrill's¹⁶ cases of children of about the same ages. We might deduce an increased oxidation of proteid tissue as evidenced by the high preformed sulphate output in its relation to total sulphur and neutral sulphur in the urine (Table 19).

Referring to the work of Schwarz,¹⁷ giving ratios of S: N in the urine, it will be seen from Table 20 that the excretion of S N in our cases is lower than those stated in the findings of this author (for a 5-year-old normal child), the amount of sulphur excreted being reduced in our cases.

GENERAL CONCLUSIONS

Most important in a consideration of the metabolism of amaurotic family idiocy is the stage of the disease and the general condition of nutrition of the patient under investigation. The two children studied by us were both in an early period of this insidious malady; their general

15. Freund: *Ztschr. f. Physiol. Chem.*, No. 29, p. 54.

16. Amberg and Morrill: *Jahrb. f. Kinderh.*, No. 69, p. 288.

17. Schwarz: *Jahrb. f. Kinderh.*, 1910, lxxii, part 5, p. 549.

nutrition was good, muscular tissue still very well preserved, and an abundant panniculus adiposus was present. So good was the general health of the children, that during the periods of observation, in both the cases a gain of weight was noted. Thus Sch. gained in the four days of the first investigation 80 gm.; in the second period 30 gm.; Patient D. F. similarly gained 180 gm. In all these instances the nourishment was well taken, the diet consisting of milk diluted in Case 2, and undiluted in Case 1. The caloric intake was in excess of the accepted figures of Heubner (100 calories per kilo per day) to maintain proper nutrition.

From a perusal of the data before us, we are struck by the fact that absorption from the gastro-intestinal tract and retention within the body are normal or even better than normal for all the constituents determined (Table 21).

In view of the fact that this disease is so prominently characterized by a marked and generalized degeneration of nerve cells and nerve tissue, as proven by the very thorough and recent histologic and pathologic studies of Schaffer,² Vogt,³ Brooks,⁴ Sachs and Strauss,⁵ and others, it would be interesting to discover in the excretions the chemical evidences of the degenerative process which we know is going on. This should be evidenced by some disturbance in the excretion of those elements which are so integral a part of nerve tissue, namely phosphorus and sulphur. In a paper dealing with the chemical analysis of the brain in two cases of amaurotic family idiocy, Mott⁷ shows a very distinct change in the relative proportions of simple and neucleoproteins, the latter being diminished, and being replaced by proteins of a simpler composition and with an increased water content. (See Mott's table.)

Close scrutiny of our figures for the intake and output of phosphorus and sulphur does not disclose a marked disturbance in the metabolism of these constituents. As has been stated, absorption and retention are unusually good and increased beyond normal, probably indicating a hyper-normal anabolic function occurring at this stage of the disease. However, when one takes into consideration the very slow process of degeneration, extending over a period of months or years, and the very small amount of actual phosphorus and sulphur in the entire cerebrospinal system, one can understand why the daily elimination of these constituents would fail to be manifested in a study of this disease for short periods and with our present methods. It would be advisable, therefore, to study the disease at intervals during its entire course, both in its earlier stages when anabolic changes apparently predominate, and in its later stages when degenerative and catabolic processes play the important rôle.

TABLE 5.—METABOLISM EXPERIMENT IN CASE 1

D. F., period four days; age 15 months; weight 8.125 kg. Nourishment equals 48 ounces of whole milk (raw), equals 975 calories per day or 120 calories per kg. of weight.

INTAKE				
Date	N	S	P	Cl
5/3	5.323	0.5447	0.8076	1.4306
5/4	7.302	0.4819	0.7890	1.3470
5/5	4.998	0.4406	0.5024	1.5590
5/6	5.702	0.5676	0.6997	1.7790
Total	23.3250	2.0348	2.7987	6.1156
Daily average 5.831		0.5087	0.6997	1.5290

OUTPUT—URINE				
Date	Amount c.c.	Acidity	NH ₃	N
5/3	490	123.9	0.1647	2.894
5/4	480	104.8	0.4000	2.432
5/6	480	100.8	0.0618	2.842
5/6	560	alk.	3.167
Total				11.335
Daily average				2.834

OUTPUT—URINE					
Date	Sulphur		Totals	P ₂ O ₅ as P	Cl
	Preformed SO ₂	Ethereal SO ₂			
5/3	0.1810	0.00578	0.2295	0.3004	0.653
5/4	0.1664	0.00817	0.1969	0.3379	0.511
5/5	0.2086	0.01262	0.2398	0.3845	0.579
5/6	0.2371	0.00239	0.2632	0.3986	0.581
Total	0.7931	0.05047	0.9294	1.4214	2.324
Daily average	0.1983	0.01262	0.23235	0.35535	0.581

STOOL			
	N	S	P
For period	0.902	0.30996	0.1969
Daily average	0.2254	0.07749	0.04922

TABLE 6.—METABOLISM EXPERIMENTS. DAILY SHEET. CASE 2

Sch., aged 7½ months; weight 7.39 kg.; nourishment, per day:

	gm. or c.c.
Whole (raw) milk	960
Water	360
Maltose	45

Caloric value=910 calories or 121 calories per kg. weight.

PERIOD I—INTAKE				
Date	N	S	P	Cl
9/19	3.3200	0.3964	0.3933	0.4700
9/20	2.8710	0.4317	0.2758	0.6700
9/31	2.4100	0.4290	0.3124	0.6600
9/22	4.2810	0.8252	0.5918	1.2100
Total	12.8820	2.0823	1.5733	3.0100
Daily average	3.2200	0.5201	0.3930	0.7530

OUTPUT—URINE							
Date	Amt. c.c.	Acidity	NH ₃	N	S	P ₂ O ₅ as P	Cl
9/19	325	143	0.273	1.2376	0.1104	0.1499	0.4499
9/20	250	102.5	0.292	1.4560	0.1047	0.1357	0.2573
9/21	215	alk.	1.0234	0.1000	0.1017	0.1526
9/22	320	alk.	1.2360	0.11498	0.0966	0.3860
Total				4.9530	0.4301	0.4839	1.2458
Daily average ..				1.2382	0.1075	0.1210	0.3115

	STOOL		
	N	S	P
For period 9/19 to 9/22, 29.5 gm. . .	0.954	0.1697	0.0413
Daily average	0.2385	0.0424	0.0104

TABLE 7.—METABOLISM EXPERIMENT. CASE 2

PERIOD II—INTAKE				
Date	N	S	P	Cl
10/13	5.61	0.915	0.936	0.937
10/14	5.34	1.092	0.896	1.312
10/15	5.984	1.191	1.493	1.461
10/16	5.505	1.139	1.144	1.303
Total	22.439	4.337	4.459	5.013
Daily average ..	5.610	1.084	1.115	1.253

OUTPUT—URINE							
Date	Amt. c.c.	Acidity	NH ₄	N	S	P ₂ O ₅ as P	Cl
10/13	730	73	0.3808	3.026	0.3927	0.1495	0.855
10/14	780	alk.	3.177	0.2986	0.3192	0.886
10/15	750	alk.	3.297	0.2133	0.2445	0.958
10/16	660	alk.	2.810	0.3025	0.3086	0.749
Total	12.310	1.2071	1.0218	3.448
Daily average	3.078	0.3020	0.2555	0.862

	STOOL		
	N	S	P
For period 10/13 to 10/16	0.305	0.336	0.771
Daily average	0.076	0.084	0.1928

TABLE 8.—INTAKE AND OUTPUT—DAILY AVERAGES

INTAKE				
	N	S	P	Cl
Sch. I	3.220	0.521	0.393	0.753
Sch. II	5.610	1.084	1.115	1.253
D. F.	5.8310	0.5087	0.6997	1.529
URINE				
Sch. I	1.2382	0.1075	0.121	0.2115
Sch. II	3.078	0.302	0.255	0.862
D. F.	2.834	0.23235	0.3553	0.581
STOOL				
Sch. I	0.2385	0.0424	0.0104
Sch. II	0.076	0.084	0.1924
D. F.	0.225	0.0775	0.0496
TOTAL OUTPUT				
Sch. I	1.4767	0.1499	0.1313	0.3115
Sch. II	3.154	0.388	0.4482	0.862
D. F.	3.059	0.3099	0.4040	0.581

TABLE 9.—NITROGEN METABOLISM. DAILY AVERAGE

	Intake	Urine	Stool	Absorption	Absorp- tion, Per cent.	Reten- tion of Intake	Per cent.
Sch. I	3.220	1.2382	0.2385	2.9815	92.5	1.744	54.15
Sch. II	5.610	3.078	0.076	5.534	98.6	2.456	43.9
D. F.	5.831	2.834	0.2254	5.6055	96.0	2.772	47.5

TABLE 10.—FIGURES FOR NITROGEN METABOLISM OF NORMAL CHILDREN (FROM SEVERAL AUTHORS) APPROXIMATELY SAME AGE AND WEIGHT AS CASE 2

	Intake	Urine	Stool	Absorption	Per cent.	Reten- tion	Per cent.
		
Rubner and Heub- ner, ¹⁰ child 7½ months	4.26	3.067	0.281	3.979	93.4	0.912	36.7
Klotz, ¹⁸ child 6 months	6.863	4.2625	0.8402	6.0231	87.7	1.76	25.6

TABLE 11.—FIGURES FOR NITROGEN METABOLISM OF NORMAL CHILDREN (FROM SEVERAL AUTHORS) APPROXIMATELY SAME AGE AND WEIGHT AS CASE 1

	Intake	Urine	Stool	Absorption	Per cent.	Reten- tion	Per cent.
		
Camerer, ¹¹ child 1 year	5.0	4.0	0.7	4.3	86	0.3	6.0
Cronheim and Meyer, ¹² child 6 months	4.454	3.182	0.530	3.923	89	0.741	16.7
Cronheim and Meyer, child 6 months	4.454	3.057	0.452	4.001	90	0.945	21.3

TABLE 12.—CHLORIN METABOLISM. DAILY AVERAGE

	Intake	Urine	Stool	Retention	Per cent.
Sch. I	0.753	0.3115	*	0.441	58.6
Sch. II	1.253	0.862	...	0.391	31
D. F.	1.529	0.581	...	0.948	62

*As HCl was added to stool in the drying process, no Cl estimations were possible.

TABLE 13.—CHLORIN METABOLISM IN HEALTHY CHILDREN (MOTHER'S MILK DIET)

	Intake	Urine	Stool	Absorption	Per cent.	Reten- tion	Per cent.
		
L. F. Meyer ..	0.3217	0.1776	0.0135	0.3162	96	0.1386	42

TABLE 14.—PHOSPHORUS METABOLISM. DAILY AVERAGE

	Intake	Urine	Stool	Absorption	Per cent.	Reten- tion	Per cent.
		
Sch. I as P	0.3930	0.1210	0.0104	0.3826	97.6	0.262	66.6
as P ₂ O ₅ 0.9039		0.2783	0.0239
Sch. II as P	1.115	0.25545	0.1928	0.9222	82.8	0.66675	60.
as P ₂ O ₅ 2.546		0.588	0.4434
D. F. as P	0.6997	0.35535	0.04922	0.6505	93	0.2951	42.2
as P ₂ O ₅ 1.609		0.817	0.1132

TABLE 15.—PHOSPHORUS METABOLISM IN HEALTHY CHILDREN (SEVERAL AUTHORS) APPROXIMATELY SAME AGES AND WEIGHTS

	Intake	Urine	Stool	Absorption	Per cent.	Reten- tion	Per cent.
		
Rubner and Heub- ner, ¹⁰ child 7½ mos., as P ₂ O ₅ 2.06		0.589	0.96	1.098	53	0.5079	24
Cronheim and Meyer, ¹² child 6 mos.	2.184	0.967	0.733	1.451	66	0.484	22
	1.872	1.069	0.671	1.201	66	0.133	7

18. Klotz: Jahrb. f. Kinderh., 1909, No. 70, p. 1.

TABLE 16.—RATIOS

	RATIOS $P_2O_5:N$.		
	Intake	Urine	Stool
Sch. I	1: 3.6	1: 4.5	1:10
Sch. II	1: 2.2	1: 5.4	1: 0.17
D. F.	1: 3.65	1: 3.4	1: 2

TABLE 17.—FIGURES FOR RATIO $P_2O_5:N$ FOR HEALTHY CHILDREN (FROM SEVERAL AUTHORS) APPROXIMATELY SAME AGE AND WEIGHT AND DIET

	Intake	Urine	Stool
Rubner and Heubner	1: 2.1	1: 5.2	1: 0.29
Keller		1: 2.1 1: 3.4 1: 3.9	
Cronheim and Meyer	1: 2.1	1: 3.3	1: 0.7
Cronheim and Meyer	1: 2.4	1: 2.8	1: 0.7

TABLE 18.—SULPHUR METABOLISM. DAILY AVERAGE

	Intake	Urine	Preformed	Ethereal	Neutral	Stool	Absorp-	Retention
	Total S	SO ₂ as S	SO ₂ as S	S	tion
Sch. I ..	0.521	0.10750424	0.4786	0.3711
.....	85 %	71.2%
Sch. II..	1.084	0.3020084	1.000	0.6985
.....	92.2%	60%
D. F. ..	0.5087	0.23235	0.1983	0.01262	0.02143	.07749	0.431	0.1989
.....	85 %	5.43%	9.57%	84.4%	39.1%

TABLE 19.—ANALYSIS OF URINES OF NORMAL CHILDREN FOR SULPHUR CONSTITUENTS. (ALL IN TERMS OF S)

	Total S	Total Sulphates	Per Cent.	Ethereal Sulphates	Per Cent.	Neutral Sulphur	Per Cent.
Amberg and Morril, child 5 mos	0.0747	0.0376	50.3	0.0371	49.7
Freund, child 6½ mos.	0.6717	0.570	86.6	0.0768	9.6	0.100	13.4
Freund, child 4½ mos.	1.032	0.773	75	0.0937	9	0.258	25

TABLE 20.—SHOWING RATIO S:N

	Intake	Urine	Stool
Sch. I	1: 6.2	1:11.6	1: 5.6
Sch. II	1: 5.2	1:10.2	1: 0.9
D. F.	1:11.7	1:12.2	1: 3

TABLE 21.—DAILY AVERAGE (PER CENT OF INTAKE)

	N	RETENTION				CL	
		N Per Cent.	S Per Cent.	P Per Cent.	P Per Cent.	.. Per Cent.	CL Per Cent.
Sch. I ..	1.744	54.15	0.371	71.2	0.262	66.6	0.441
Sch. II ..	2.456	43.9	0.6985	64.4	0.6665	60	0.391
D. D. ..	2.772	47.5	0.1989	39.1	0.2951	42.2	0.948
ABSORPTION (PER CENT. INTAKE)							
Sch. I ..	2.9815	92.5	0.4786	91.7	0.3826	97.6
Sch. II..	5.534	98.6	1.000	92.2	0.9222	82.8
D. F. ..	5.6055	96	0.431	84.8	0.6535	93

PROGRESS IN PEDIATRICS

A SUMMARY OF THE RECENT LITERATURE ON ORTHOSTATIC ALBUMINURIA

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In May, 1910, D. R. Hooker¹ published a critical summary of the literature on the subject of orthostatic albuminuria. In this excellent paper in which he gives a concise, comprehensive and systematic review of the various theories which have been advanced to explain this type of albuminuria, he divides the subject-matter into three periods. The first period deals with the work of Leube, Senator, Posner, Ultzman, Gull, Moxon and others, who first laid emphasis on the presence of albumin in the urine of healthy individuals; it includes Pavy, who, in 1885, was the first to show the influence of the upright posture, and ends with the paper of Dubreuilh, in 1887. The second period extends from 1887 to the appearance of Edel's researches in 1904. In this period falls some of Teissier's work in which the name "orthostatic" is first applied. "This period is characterized by the development of scientific interest and a strong effort to define the etiology of albuminuria by means other than simple clinical observation." The third period includes the work of Teissier, who first emphasized the occurrence of true orthostatic albuminuria where no etiologic factor can be found, and the cause of which he believes to lie in the semipermeability of the glomeruli, due to faulty development. In this period also appear the researches of Erlanger and Hooker, who showed the relationship between the vasomotor system, especially the pulse-pressure and albuminuria; and also the work of Langstein, who first studied the metabolism of orthostatic albuminurias and who published the first autopsy on an undoubted case.

LORDOSIS AS A CAUSE OF ALBUMINURIA

Since the publication of Hooker's review, however, the subject of orthostatic albuminuria has received added interest and much new work has appeared as the result of the publishing of Ludwig Jehle's monograph on Lordotic Albuminuria.² Jehle believes the appearance of albumin in the urine while the individual is in the upright position and its disappearance on lying down is due to a venous hyperemia of the

1. Hooker, D. R.: Arch. Int. Med., 1910, v, 491.

2. Jehle, L.: Die Lordotische Albuminurie. Leipzig and Wien, 1909.

kidney brought about by a faulty position of the lumbar spine. He observed that orthostatic albuminurics showed a lordosis in the region of the first and second lumbar vertebrae. He bases his views on the examination of a large number (300) of children and attempts to show that the lordosis is practically the only factor of importance. By causing an artificial lordotic position of the spine he can produce albuminuria with the child on its back, while on the other hand, by the application of a plaster jacket so as to correct the lordosis, he is able to make the urine albumin-free even when the child is up and about. By the use of a specially constructed apparatus he can reproduce on paper the exact contour of the spinal column and can show that those children that had previously been diagnosed as orthostatic albuminurics all present the typical lordosis. Conversely children whose vertebral columns are straight fail to show albumin in their urine.

Jehle's contention that the lordotic lumbar spine is the chief cause of the albuminuria has been corroborated by some investigators and denied by a few. Fischl³ agrees with Jehle in considering the lordosis of great importance, but he believes that there is still another factor to be dealt with in the shape of a peculiar weakness of the kidney which permits the lordotic posture to produce albuminuria. This is especially emphasized in the difficulty with which albuminuria is obtained in normal children by placing them in artificial lordosis. He is not inclined to attribute too much importance to the vasomotor theory, since the results of blood-pressure readings, sphygmograms and x-ray examinations have varied greatly with different authors. He concludes "that under the influence of a lordosis, limited to the upper lumbar column and appearing with the body in certain positions, a congestion of the kidneys is brought about which, in the presence of an existing disposition of these organs to mechanical influences, leads to an excretion of albumin and formed elements, the intensity of this excretion depending directly on the grade and duration of the procedure." He therefore would name the condition "*Lordotische dispositionsalbuminurie*."

M. Engländer,⁴ in reporting a case in an adult, takes this same standpoint, that there must be a second etiologic factor besides the lordosis. Hamburger⁵ in the same way, while conceding the importance of the purely mechanical factor, points out that vasomotor instability must play a part, and that it is chiefly in vasoneurotics that lordosis produces albuminuria. He emphasizes the fact that the same individual reacts to lordosis at one time with an albuminuria, at another time without it.

3. Fischl, R.: Arch. f. Kinderh., 1909, lii, 261.

4. Engländer, M.: "Ein Fall von orthotischer Albuminurie." Mitt. der Gesellsch., f. inn. Med. u. Kinderh. in Wien, 1911, p. 166.

Fischl⁶ has, moreover, confirmed the importance of lordosis by animal experiments. Rabbits, when kept in exaggerated lordosis, showed albumin, casts and red blood-cells. Food given seemed to influence the results. Repeated experimental lordosis may lead to nephritis and death. The kidneys of such cases pathologically examined resemble the kidneys of padonephritis. In dogs, also, albumin appeared after lordosis. The lordosis seems to act mechanically and not reflexly, since it also provokes albuminuria when the whole experiment is carried on in narcosis. The general blood-pressure does not seem to have much influence on the excretion of the albumin, but the oncometer shows an increase in the volume of the kidney, and as increase in the arterial flow can be excluded, this probably means a slowing of the blood-current in the kidney.

Together with Wohrizek,⁷ Fischl has used a corset, which cures not only the albuminuria, but also the attending symptoms.

Bruck⁸ also emphasizes the importance of lordosis as a causative factor, finding it in almost every case of orthostatic albuminuria. He was, however, in contradistinction to Jehle, unable to obtain albuminuria in the prone position no matter how great an artificial lordosis he produced. He took normal non-lordotic children and put them in lordotic position by letting them kneel. Of the forty-four children thus examined, 18 per cent. showed albumin. Some of these positive cases were absolutely normal children, some had organic disease, some were markedly neuropathic. In general, he concludes that "albuminuria provocativa orthostatica" (i. e., albuminuria which does not appear until it is provoked by placing the child in an upright lordotic position), though an interesting condition, cannot in any manner be used to differentiate various types of children nor to distinguish various degrees of renal sufficiency.

B. Vas⁹ reports observations on 150 girls ranging in age from 9 to 14 years. Of these, sixty-two had albuminuria, and twenty-six of these showed the orthostatic variety. Examining these twenty-six he found albumin together with lordosis in fifteen cases; albumin without lordosis in eleven cases. He also found nine cases with lordosis, but without albuminuria. He concludes that at puberty orthostatic albuminuria occurs about as often with lordosis as without it. Lordosis without albuminuria also occurs. It cannot be regarded as the sole cause of orthostatic albuminuria.

5. Hamburger, F.: *Wien. klin. Wchnschr.*, Feb. 15, 1912, No. 7.

6. Fischl, R.: *Ueber mechanische Hervorrufung von Albuminurie u. Erzeugung von Nephritis bei Kaninchen*, *Monatschr. f. Kinderh.*, 1909, viii, 388, and 1910, p. 641.

7. Wohrizek: *Med. Klin.*, May 1, 1910.

8. Bruck, A. W.: *Ueber Albuminuria Provocativa Orthostatica*, *München. med. Wchnschr.*, 1908, No. 44, p. 2271.

9. Vas, B.: *Zur Frage der lordotischen Albuminurie*, *Deutsch. med. Wchnschr.*, 1909, No. 34.

There seems to be a great difference of opinion as to whether the assumption of the lordotic position while lying down gives rise to albuminuria or not. Bury and Ward¹⁰ report a case of chorea and postural albuminuria, in which they could get only inconstant traces of albumin when lordosis was assumed with the child in bed. Hutinel¹¹ reports contradictory results. Turrettini,¹² on the other hand, finds that exaggeration of the lumbar lordosis causes the appearance of albumin in all cases of orthostatic albuminuria regardless of the position — whether horizontal or standing. He finds that even while standing the assumption of a position with the trunk bent slightly forward is sufficient to remove the albumin again. F. Parkes Weber,¹³ and also Nobécourt,¹⁴ reporting cases, also concede that lordosis has a marked effect, but that nevertheless there are still other causative factors at work.

Ebstein¹⁵ calls attention to an article written by Bartels in 1875, in which he reports a case of pseudohypertrophic muscular dystrophy with marked lordosis and an albuminuria of the typical orthostatic variety. Goldreich¹⁶ reports a similar case in a child, aged 9 years, in whom the same muscular disease was present, accompanied by lordosis and orthostatic albuminuria. Schreiber,¹⁷ on the other hand, describes thirty cases of coxalgia with lordosis, none of which showed albuminuria; while Pechowitsch¹⁸ found that in a class of thirty lordotic children who were being treated by Klapp's creeping exercises, five showed albuminuria. All of these five showed less albumin immediately after treatment by exercises which diminished their lordosis.

A very good exposition of the relationship of lordosis to albuminuria is presented by Pincherle,¹⁹ and is worth reporting in more detail. He examined over 100 children and comes to the following conclusions: Undoubtedly a lordosis not too extreme in character and involving the

10. Bury and Ward: A Case of Postural Albuminuria in a Boy the Subject of Chorea, *Lancet*, London, Jan. 1, 1910.

11. Hutinel: Albuminurie orthostatique, *Rev. gén. de clin. et de therap.*, 1910, p. 372.

12. Turrettini, G.: Etude clinique de l'albuminurie dite orthostatique, *Rev. méd. de la Suisse romande*, 1910, No. 30, p. 767.

13. Weber, F. P.: Remarks on Orthostatic albuminuria, *Brit. Jour. of Child. Dis.*, September, 1911.

14. Nobécourt: Albuminurie orthostatique Fonctionnelle, *Gaz. d. hôp.*, 1910, p. 313.

15. Ebstein, E.: Juvenile Dystrophie und lordotische Albuminurie im Kindesalter, *Ztschr. f. Kinderh.*, 1911, No. 3.

16. Goldreich, A.: Dystrophia musculorum progressiva mit lordotischer Albuminurie, *Mitt. d. Gesellsch. f. inn. Med. u. Kinderh. in Wien*, 1911, No. 7, p. 135.

17. Schreiber, M. G.: Critique de la Théorie Lordotique de l'Albuminurie Orthostatique, *Presse méd.*, Oct. 20, 1909.

18. Pechowitsch, G.: Einfluss der Kriegsstübungen auf die lordotische Albuminurie, *Deutsch. med. Wchnschr.*, Oct. 27, 1910.

19. Pincherle: *Riv. di clin. pediat.*, 1911. Reviewed in the *Monatschr. f. Kinderh.*, 1912, No. 11, p. 508.

upper segment of the lumbar column, is a marked factor in causing albuminuria. There is no direct relationship between the grade of the lordosis and the albuminuria. In some individuals with a marked lordosis it was impossible even with artificial exaggeration of the deformity to cause albumin to appear. Artificial lordosis of moderate grade, however, in most cases results in albuminuria, whether in the vertical or the horizontal position. This reaction to posture differs; in normal individuals the albumin excreted is minimal in amount; in those predisposed (nephritics, tuberculous individuals) it is much greater in amount. The reaction to lordosis is characterized by albuminuria, oliguria and the appearance of formed elements in the urine; it varies with the mechanical factor, the general condition of the subject and with the local condition in the kidney. The traumatic influence of the lordosis may show the weakness left by previous disease, and the reaction to posture may therefore, as pointed out by Nothman and Devoto, be useful as a functional renal test. Attention to an existing lordosis is often an important factor in curing an albuminuria. The damaging influence of lordosis on the kidney is shown by animal experiments in which staphylococci were injected in control and into lordotic rabbits, with the result that the latter got very much more severe renal lesions.

Goetzky,²⁰ after careful examination of a number of children over a considerable period of time, is inclined to deny the significance of lordosis as the etiologic factor in true orthostatic albuminuria. He admits that by artificial lordosis one is able to produce an albuminuria in almost every child, whether healthy or ill, but he cites orthostatic cases who show no trace of lordosis and also points to the fact that the degree of lordosis and the amount of albumin are not at all proportional. The albumin in cases of orthostatic albuminuria disappears almost immediately when the patient assumes the horizontal position, whereas after artificial lordosis albuminuria may persist for five or six hours.

OTHER MECHANICAL FACTORS

Other mechanical factors besides the lordosis have been pointed out as causes of the albuminuria. Eppinger,²¹ in reporting the case of an adult suffering from orthostatic albuminuria, shows that the distance between the upper border of the heart and the diaphragm, as revealed by the x-rays, is increased; that is to say, the position of the diaphragm is very low. As a result of this, when the patient is in the upright position, there is tension on the inferior vena cava and consequent stasis in the renal

20. Goetzky, F.: Zur Kenntniss der orthotischen Albuminurie, Inaugural dissertation, Berlin, 1910.

21. Eppinger: Die Function des Zwerchfells beim Zustandekommen der orthostatischen Albuminurie, Mitt. d. Gesellsch. f. inn. Med. u. Kinderh. in Wien, 1912, No. 6.

veins. Eppinger believes that the disappearance of the albumin after the application of an abdominal binder is due to the resulting elevation of the diaphragm.

Vorpahl²² describes a 12-year old girl with orthostatic albuminuria who presented slight lordosis, but marked left lumbar scoliosis. In the sitting posture, which overcame the lordosis, albumin persisted. Ureteral catheterization showed that the albumin came from only the right kidney, evidently as a result of the scoliosis.

Mayer²³ reports an orthostatic case in an adult in whom ureteral catheterization also showed unilateral albuminuria.

Piesen²⁴ comments on the frequency of orthostatic albuminuria in school children who are forced to sit with their arms folded behind their backs.

A number of cases have been reported (Niviere,²⁵ Mosny,²⁶ Lury²⁷), in which orthostatic albuminuria seemed to be dependent on movable kidney, as was long ago pointed out by Sutherland.

RELATIONSHIP OF ORTHOSTATIC ALBUMINURIA TO ACUTE DISEASES, ESPECIALLY TO SCARLET FEVER

Stephanie Weiss-Eder²⁸ let children suffering from scarlet fever kneel so as to produce lordosis for ten to twenty-five minutes. She repeated this procedure every two to seven days, using only children who, in the non-lordotic position, showed no albumin. Of forty children thus examined, twenty-three showed albumin and seventeen showed none. In none of the twenty-three positive cases did a nephritis follow. One child, which in lordosis was continuously negative, developed a nephritis on the twenty-third day. The author concludes that (1) children, who in convalescence from scarlet fever have orthostatic albuminuria, are not more disposed to nephritis than other children; (2) children convalescent from scarlet fever having nephritis often show orthostatic albuminuria which may be due to weak muscles; (3) 57.5 per cent. of the children convalescent from scarlet fever show orthostatic albuminuria.

These results (and also those of a number of other authors) are not in accord with the findings of Nothman,²⁹ who believes that the artificial lordotic position may be used to give information concerning the func-

22. Vorpahl, K.: Ueber einseitige orthostatische Albuminurie, Berl. klin. Wehnschr., May 2, 1910, p. 827.

23. Mayer, K.: Einseitige Zyklische-orthotische Albuminurie, Ztschr. f. gynäkolog. Uro., 1909, i, 229.

24. Piesen: Wien. klin. Wehnschr., Jan. 5, 1911.

25. Niviere: Soc. méd. d. hôp. de Paris, 1904.

26. Mosny: Soc. méd. d. hôp. de Paris, 1904.

27. Lury: Jahrb. f. Kinderh., December, 1910.

28. Weiss-Eder, S.: Orthotische Albuminurie und Scharlachnephritis, Wien. med. Wehnschr., 1909, No. 18, p. 977.

tional efficiency of the kidney. He found that in twelve out of thirteen cases of scarlet fever in which at an earlier date the lordotic experiment was positive, albumin later on appeared in the urine; but in those in whom lordosis did not cause albuminuria, albumin never appeared spontaneously later on. He thinks that just as nephritis may terminate in orthostatic albuminuria, so conversely an orthostatic albuminuria may be the first sign of a nephritis, and that on this account convalescents from scarlet fever showing albumin after kneeling need particular watching in respect to developing nephritis.

Schick²⁹ comments on the good prognosis of orthostatic albuminuria following scarlet fever. He refers to Jehle, who examined seventeen children in various stages of scarlet fever. In twelve of these there was marked albuminuria during lordotic positions whether upright or prone, but in none of them did a nephritis supervene.

Le Noir³¹ had a patient with orthostatic albuminuria who passed through an attack of typhoid and then one of scarlet fever without developing symptoms of renal involvement. Dufour³² reports a similar case in which previous orthostatic albuminuria followed by scarlet fever showed no sign of nephritis. Turrettini³³ describes similar cases. In a series of fifty scarlet fever cases reported by him, four had signs of nephritis. In these four children, the creation of an artificial lordosis by placing a pillow beneath the lumbar spine, caused a recrudescence of the nephritis lasting several days.

RELATION TO TUBERCULOSIS

The relationship between tuberculosis and albuminuria has long been pointed out especially by the French, who speak of a pretuberculous albuminuria. Lately various French observers have emphasized that orthostatic albuminuria occurs more often in children with a tuberculous family history. F. Parkes Weber,¹⁸ on the other hand, believes that it is merely the similarity in the clinical pictures presented by orthostatic albuminurics and tuberculous individuals (tall, thin, flat-chested individuals; winged scapulæ, etc.), which has given rise to the opinion that the albuminuria may be the result of the infection. Goetzky²⁰ in a large number of cases was also unable to find a greater number of positive Pirquet reactions in children suffering from orthostatic albuminuria than in control children.

29. Nothman, H.: Ueber lordotische Albuminurie, *Arch. f. Kinderh.*, 1909, No. 49, p. 216.

30. Escherich and Schick: *Sharlach*, 1912, Nothnagel's System, p. 141.

31. Le Noir: Quoted by Courcoux, *Paris méd.*, 1910-11, p. 363.

32. Dufour, H.: *Soc. méd. d. hôp.*, Feb. 2, 1906.

33. Turrettini, G.: De la Pathogenie de l'Albuminurie dite Orthostatique, *Rev. de Méd.*, September, 1909, p. 694.

Ludke and Sturm,³⁴ however, conclude from a study of 140 cases that a large percentage of individuals with pulmonary tuberculosis show albumin in their urine after being on their feet for one hour. In those cases in which no albumin appeared, a very small injection of tuberculin resulted in an albuminuria in more than half of the cases. The authors believe that orthostatic albuminuria can be used as a diagnostic aid in early tuberculosis.

ORTHOSTATIC ALBUMINURIA AND RENAL SUFFICIENCY

Considerable confusion exists as to the relationship between orthostatic albuminuria and nephritis. Heubner and his school believe that a case may be classed as orthostatic albuminuria only if the presence of albumin conforms strictly to the posture of the child and if formed elements are continuously absent. Goetzky, in his monograph before referred to, published from Heubner's clinic, divides his cases into: 1. Orthostatic albuminurics, in whom there are never any casts and in whom the presence of albumin is always dependent on posture. 2. Orthostatic nephritics, in whom casts may appear, but who seem much influenced by posture. 3. Cases in which the albuminuria is not strictly dependent on posture and which may show casts. (These last are cases of chronic pædonephritis.) He still adheres to the belief that the appearance of casts and red blood cells signifies the existence of a nephritis, and that therefore Jehle's contention that formed elements appear after artificial lordosis is true only because Jehle was dealing with kidneys the seat of previous inflammation. In other words, many of Jehle's experiments were performed not on normal children, but on chronic nephritics of the type pointed out by Heubner as characterized by no subjective or objective symptoms excepting the excretion of urine containing albumin and occasional casts.

The French school, following the lead of Teissier, also insist on a rigid classification separating the true orthostatic albuminuria from the other forms. Nobécourt¹⁴ reports cases in which tests for functional efficiency of the kidney (methylene-blue and NaCl excretion) were normal. He believes that orthostatic albuminuria is due to changes in the blood-supply of the kidneys. According to Springer,³⁵ the condition is due probably to a relative insufficiency of the kidney caused by rapid growth of the rest of the body, with which the growth of the kidney is unable to keep pace. In favor of this view are the following facts: The disease appears as a rule at or near puberty. It is frequently accompanied by

34. Ludke, H., and Sturm, J.: Die orthotische Albuminurie bei Tuberculose, München. med. Wchnschr., May 9, 1911.

35. Springer, M.: Albuminurie Physiologique et Orthostatique, Presse méd., July 29, 1911.

symptoms of vasomotor insufficiency. It tends to heal spontaneously when the time of rapid growth is past. Similar views are put forth by Turrettini,³⁶ who believes that true orthostatic albuminuria is due to lordosis acting on a kidney insufficient because of rapid growth.

Courcoux³⁶ gives a very clear classification of the cases, dividing them as follows: 1. True, so-called functional, albuminurias, usually in tall, thin children, 10 to 15 years of age; lordotic or scoliotic; emotional, easily tired, complaining of headaches, and showing a neuropathic heredity. Their complaints point to vasomotor instability as shown by cold, clammy extremities, lability of the pulse, palpitation, etc. Casts are never found in their urine. Albuminuria is most marked toward the end of the morning. Functional renal tests are normal. Outcome of the disease is good and the kidneys are not more susceptible to damage even by scarlet fever. 2. Orthostatic nephritic albuminuria. This is the commonest type. It also usually occurs in children (a) as the result of an infection, (b) as the preliminary symptoms of a chronic nephritis. These cases may resemble the first variety, but functional renal tests show insufficiency. As a result of errors in diet or fatigue, continuous albuminuria may occur. The urine shows diminution in the excretion of nitrogen, chlorids and phosphates, and reveals an oliguria in the upright position. When frequently examined casts are found. 3. So-called associated orthostatic albuminuria—these are cases associated with gastro-intestinal disturbances. Courcoux believes that in any of these three classes albumin appears in the upright posture owing to diminished blood-supply to the kidney, and that this diminution occurs especially commonly in persons showing vasomotor instability.

In a series of articles Linossier and Lemoine³⁷ lay great stress on the oliguria which occurs in cases of orthostatic albuminuria. By a number of careful researches they come to the conclusion that the functional efficiency of the kidneys of such patients can best be appreciated by the measurement of this oliguria. They find that in a kidney the seat of very slight disease, the upright posture causes an oliguria accompanied by a diminution in the excretion of chlorids, urea and phosphates. This orthostatic oliguria in its more advanced stage may become an albuminuria. Normal persons show no orthostatic oliguria. The authors conclude that the oliguria and the consequent albuminuria are caused by a slowing of the renal circulation brought about by the upright posture; and that

36. Courcoux: *Die Orthostatischen Albuminurien*. Translated from *Paris méd.* by G. Steinitz in *Allg. Wien. med. Ztg.*, 1911, p. 324.

37. Linossier, G., and Lemoine, G. H.: *Le mécanisme de l'albuminurie et de l'oligurie orthostatique*, *Presse méd.* Mar. 24, 1909; also *Soc. méd. d. hôp.*, Mar. 19, 1909, p. 565.

they are due to some alteration in the kidney, probably more of a functional than an organic nature.

NATURE OF THE ALBUMINOUS PRECIPITATE

For a number of years the fact has been known that in the urine of orthostatic albuminuria cases an abundant precipitate is thrown down on the addition of acetic acid in the cold. The nature of this precipitate has been disputed. Langstein³⁸ believed it was probably of the nature of euglobulin, and that on account of the very small amounts of phosphorus it contained, it was not a nucleoproteid as had been supposed. Lately Pollitzer³⁹ has published work which corroborates the theory of Moerner that the precipitate is caused by a combination of serum-albumin and chondroitin-sulfuric acid. Pollitzer used serum-albumin as a titration fluid and showed that when this was added to normal or to nephritic urine, only a very faint opalescence appeared. When, however, it was added to the evening urines of orthostatic albuminuria cases a heavy precipitate resulted. This evidently means that there is present in such urine a body, possibly chondroitin-sulfuric acid, which in the presence of acetic acid in the cold, unites with serum-albumin to form an insoluble compound.

Giffhorn⁴⁰ found that in the urines of infants suffering from malnutrition or dyspeptic disturbances a precipitate often appeared on adding acetic acid in the cold. However, he does not believe that its presence is of much significance.

PROGNOSIS

In general, recent literature lays stress on the good prognosis of true orthostatic albuminuria. In a discussion of the after-history of orthostatic cases at the Royal Society⁴¹ in London, numerous examples of the condition were cited to show that its prognosis was excellent. Hutinel¹¹ and F. P. Weber¹⁸ lay particular stress on the good outcome of the disease, the latter believing that even the presence of an occasional hyaline cast is of no significance. This is contrary to the views expressed by Heubner and his adherents, who, as has been mentioned above, believe that the presence of casts speaks for a nephritis and therefore for a more

38. Langstein, L.: *Die Albuminurien älterer Kinder*, Monograph, Leipzig, 1907.

39. Pollitzer, H.: *Ueber die Natur u. die Rolle des durch Essigsäure fällbaren Eiweisskörpers bei orthotischen Albuminurien*, Deutsch. med. Wchnschr., March 14, 1912.

40. Giffhorn: *Beitrag zur Klinischen Bedeutung des durch Essigsäure fällbaren Eiweisskörpers im Urin der Säuglinge*. Monatschr. f. Kinderh., 1911, p. 648.

41. *The After-History of the Albuminuria of Adolescence*. Brit. Med. Jour., May 6 and 13, 1911.

serious prognosis. In this connection it is of interest that recently C. Posner⁴² has expressed his view that occasional hyaline casts may be present without a real inflammation of the kidney.

TREATMENT

In all the recent writings nothing has been added to the therapeutics of orthostatic albuminuria with the exception of mechanical and gymnastic measures used to overcome any existing lordosis, as referred to above.

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METABOLISM AND NUTRITION

Medical Certification of Milk; Its Advantages in Infant Feeding

(G. C. Mosher: *Dietetic and Hygienic Gazette*, March, 1912)

The most essential feature of the infant feeding reform, in the opinion of Mosher, is education; education of the profession and through it of the nurses and mothers. When it is stated in a newspaper article that a certain specimen of milk contains 5,000,000 bacteria to the cubic centimeter, few people stop to consider what it signifies, he says; but where we translate the language to the vernacular, and say that the specks in the bottom of the milk bottle are cow manure and dead epidermis from the cow's body, falling into the milk-pail during the faulty process of milking, it becomes more tangible and the enormity of the offense appeals to any layman. In every community there has often been sold milk at a high price under the name of "baby milk," or some such title as would indicate the milk to have some special qualification. As a matter of fact, these claims are frequently not based on any more ground than that the mothers of children fed on this milk have confidence in the dairyman, and pay him the excess price because of this confidence, the milk usually having been taken from the same can as that called commercial or table milk. In other words, the child fed on this milk was usually running the same risks as every other baby fed on herd milk, and the basis of security which the mother imagined was a real protection because she paid for the "baby milk" a price which often she could not afford, caused her to become the victim of misplaced confidence.

Some of the points of the series of minimum requirements adopted by the Kansas City Pure Milk Commission are that the barns shall be of sanitary construction, with a proper area of cubic feet for each animal; a system of ventilation to insure pure air in the stable; pure water-supply; cement floors and trenches, to be flushed daily with running water. The building must be ceiled to prevent accumulation of dust over the cows. The cows are quarantined until passed on by the commission veterinarian before being added to the herd. The fresh cow is not to be milked for use in the milk-supply until about the fifth day after her delivery. The milk is discarded six weeks before her next calving; cows are fed after milking, so as to avoid dust during milking. The cows are all washed over the udder and flank rubbed dry; then a chain passed

42. Posner, C.: Die diagnostische u. prognostische Bedeutung der Harnsedimente. Samml. Zwangloser Abhand. a. d. Grenzgeb. d. Verdauungskr. u. Stoffwechsel, 1912, iii, No. 7.

under their necks to prevent their lying down until after milking is finished, to avoid soiling the udder. Sanitary suits are worn by the milkers, and the hands must be washed and wiped dry before each milking. The pails used have small openings in the top to prevent the entrance of any foreign material. The first few spurts are always discarded, which insures a diminution of bacterial contamination. The milk of each cow is at once carried to the dairy house, and not allowed to remain in the warm stable after being drawn. The milk is to be bottled under most careful auspices and sealed by the official seal of the commission, which guarantees it to the consumer. The commission has adopted as a maximum bacterial count 30,000 to the cubic centimeter for all bacteria. Certified milk is not treated in any way to preserve it. Nothing is added to it or taken from it. It is simply pure milk, kept from its origin until the delivery to the customer.

F. C. ZAPFFE.

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THE INFLUENCE OF HIGH PROTEIN FEEDING ON THE GENERAL METABOLISM, ON THE INTESTINAL FLORA AND ON THE BODY TEM- PERATURE OF INFANTS *

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PART I.—GENERAL CONSIDERATIONS

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A scrutiny of the extensive data obtained from the metabolic study of infants in a state of chronic malnutrition reveals the fact that the fundamental condition is a lack of utilization by the organism of nourishment. Despite the high calorific value of the diet, there is no increase in body weight. The cause of this imperfect utilization has not yet been established. It seemed to us that there was one possible factor, the study of which has been particularly neglected, namely: the correlation of the influence of intestinal bacterial flora and the utilization of the ingested foodstuffs. An investigation of this question was the original object of the work undertaken in this study. It was planned to alter the diet of the infants in a manner that in different periods it would contain a maximum of one of the three principal food constituents—protein, fat or carbohydrate—and a minimum of the other two. This plan was carried out in one series of observations. The infant was placed on a diet of modified milk containing 2.6 per cent. fat, 3 per cent. sugar and 2.4 per cent. protein. This was continued for about three weeks. It served to determine the normal flora for this child. The diet

*From the Laboratories of the Rockefeller Institute for Medical Research, and the Babies' Hospital, New York.

was then changed to a milk formula containing 0. per cent. fat, 6 per cent. sugar and 3.5 per cent. protein, and later to one with 2.9 per cent. fat, 1.5 per cent. sugar and 5.8 per cent. protein.

It was observed that under the influence of these changes in diet the bacterial intestinal flora was modified both qualitatively and quantitatively. The changes are described in detail in Dr. Wollstein's paper (Part III). The gratifying feature of the observations was the marked general improvement noted during the period of high protein intake. The general condition of the infant was better than in any of the preceding periods, and the stools acquired a normal appearance, which is so rare in conditions of chronic malnutrition and which in this patient they had not previously shown.

It was intended to repeat this study on a greater number of infants. However, an unexpected observation caused us to abandon the original plan of the work and direct our energies for the present toward the analysis of that observation. This was the abrupt development of fever and nervous symptoms during the period of high protein intake, under conditions which led to the suspicion that the food given might be the cause of these phenomena.

Finkelstein¹ was the first to revive the interest of the pediatricist and the general physician in febrile conditions that are caused not by infection nor by products of bacterial action. He observed that some of the fundamental food constituents that are essential for maintenance of life and growth of the organism, may, under certain conditions, exert a definite toxic effect in so far as to cause fever and other attendant symptoms of a fairly uniform character. His views were based at first on clinical observations and were later corroborated experimentally in his laboratory by his associates, principally by L. F. Meyer.² On the basis of both experimental and clinical evidence the following conclusions were formulated:

1. The normal food of infants contains what he designated as "pyretogenic" and "apyretogenic" elements.
2. The sugars and salts belong to the first group.
3. Casein and other proteins belong to the second group and never give rise to fever.
4. The fever produced by sugar and salts is due to the direct action of these substances, and not to their influence on the bacterial flora.
5. In perfect health, neither salt nor sugar, even when given in considerable excess of the normal requirement, produces any disturbance of the body temperature.
6. It is the function of the intestinal wall and of the liver to keep in check the toxic tendencies of salt and of sugar.

1. Finkelstein, H.: *Deutsch. med. Wchnschr.*, 1909, v, 190.

2. Meyer, L. F.: *Deutsch. med. Wchnschr.*, 1909, v, 194.

Our observations apparently contradicted the conclusions of Finkelstein regarding casein, and hence it became important to make certain whether or not the fever in our patient was caused by some unknown accident or was actually due to the casein intake. The subsequent observations were planned with a view of furnishing evidence in support of or against the pyretogenic influence of casein. The bacteriological studies were continued, as it was hoped that through them also some information might be obtained that would enable us to determine whether the rise of the body temperature accompanying the high intake of casein was the result of a direct action of the protein or indirectly due to its influence on the intestinal flora.

The circumstances under which the rise of body temperature first occurred were the following: In order to secure a diet containing the maximum part of the calorific requirement in form of protein, milk had to be avoided as the solvent of the casein, as such a mixture generally gave too high a calorific value to the food. The casein was therefore dissolved with the addition of a solution of sodium hydrate; the final mixture being, however, rather on the acid than on the alkaline side. This preparation (for details on composition see Miss Courtney's paper) is referred to subsequently in this article as the "synthetic" food. It varied slightly in its percentages when prepared at different times; its average composition was, however, fat, 2 per cent.; sugar, 1.8 per cent.; protein, 6 per cent.

On the fourth day, while taking this food, the infant abruptly developed high fever, great restlessness and other symptoms of discomfort, which ceased as soon as the food was changed.

Careful and repeated physical examinations of the infant were made, but failed to reveal any pathologic condition of the internal organs to which the fever could be attributed. Hence, attention was again directed to the composition of the food during the "synthetic" period and during that of the high protein intake which immediately preceded it. The only important difference appeared to be a reduction in the amount of whey added. For six days this child had taken a milk formula containing 5.5 per cent. protein without showing the slightest disturbance. On the contrary, he was happy, comfortable and gaining in weight; but on the fourth day, on the "synthetic" diet, fever and its attendant symptoms were seen.

The same observation was repeated on this child two months later, with results which were practically identical. After the temperature had been normal for a long time and the child to all appearance well, he developed, on the sixth day after beginning the "synthetic" food, high fever, accompanied by the symptoms previously seen. All these, as before, disappeared immediately with the change in food.

Observations on another infant gave essentially the same result. In this patient the protein percentage in the milk formula was gradually raised in the course of thirteen days from 4 to 6 per cent. It was kept at the latter figure for six days. During all of this period of high protein feeding, lasting nineteen days, the child remained well and gained weight. The "synthetic" food formula was then substituted, and promptly on the fourth day thereafter the child responded with an attack of fever. Since the symptoms were not so severe in this patient, the food was not changed as soon as fever occurred. As rather marked constipation existed, castor oil and then calomel were administered to determine whether or not constipation might be a factor. But the temperature was not influenced by the catharsis. Finally, on the seventh day of the fever, the food was discontinued and a simple milk dilution substituted. Immediately the temperature fell to normal and remained there.

On a third infant two observations were made. In the first one the protein percentage in the milk formula was gradually raised from 4 to 6 per cent. during a period of ten days. It was kept at the latter figure for five days longer. During this time there was no fever or sign of disturbance and a slight gain in weight. On the fifth day, after a change was made to the "synthetic" food, fever and the usual symptoms developed, ceasing at once when the food was changed to a simple milk dilution.

In a second observation on this infant a milk formula containing 6 per cent. protein was continued for sixteen days without fever or abnormal symptoms; but fever developed on the fifth day after a change was made to the "synthetic" food, which contained the same percentage of protein.

From the standpoint of metabolism, the only striking thing accompanying the fever was the complete retention of the chlorids. This was seen in all the cases. It began two or three days before the rise in temperature occurred and continued into the febrile period. The nitrogen retention was good, and the proportion of ethereal sulphates in the urine did not differ strikingly from the values obtained in other periods.

ANALYSIS OF THE FACTORS THAT MIGHT HAVE BEEN INSTRUMENTAL IN CAUSING THE FEVER

That its occurrence was not accidental seems established by its regular development in every observation at approximately the same time after beginning the "synthetic" food; also by the fact that although these patients were under observation for several months, no similar attacks were seen under other conditions; nor was there evidence in any case that the fever was due to intercurrent illness as a complication.

This possibility was always borne in mind; the patients were frequently examined and watched for local symptoms of every sort. As already mentioned, in only one case was constipation marked, and in this patient free catharsis did not influence the fever. Furthermore, the stools in most of the observations, both before and during the fever, were quite normal.

The changes in the intestinal flora were very similar in all the observations. There was a very great reduction in the number of fermentative organisms (it will be remembered that in all the cases the percentage of carbohydrates in the food was low, usually 2 per cent. or less), and a great increase in the proteolytic varieties. That the fever was due to infection from the latter seems highly improbable for several reasons: The flora during the attack did not differ essentially from that which existed for several days before and several days after the fever; the symptoms developed very acutely, and if the food was at once changed they ceased almost immediately; furthermore, the stools gave no evidence of any such infective process.

The rise of temperature invariably occurred after the "synthetic" food had been given and on no other diet, and that it came regularly in each case after the food had been taken for about the same length of time, points strongly to the food as the cause of the temperature. What was it in the food, then, which brought about this result? Was it simply cumulative effect of previous high protein feeding, or was it something in the "synthetic" food mixture?

The first hypothesis seems disproved by two of the observations. Whereas, in the others the temperature occurred in about ten days after beginning the high protein feeding, in two instances very high protein (in one child, between 5 and 6 per cent. for eleven days, in the other 6 per cent. for sixteen days) had been given without producing fever or other abnormal symptoms. Yet in both fever developed on the fourth day after the change was made to the "synthetic" formula.

The "synthetic" food formula did not differ essentially in the percentage of fat, sugar and protein from the food which immediately preceded it and which produced no fever. On the contrary it was the aim to make the percentages in the two foods as nearly identical as possible. The only difference was in the mode of preparation. To the "synthetic" food to effect a solution of the casein in the minimum amount of whey, sodium hydrate was added. The daily amount used was about 1 gm. In spite of this addition the total salt intake of the infant while on the "synthetic" food differed but little from that taken in the period immediately preceding. Thus the average salt intake of Case 1 for ten days before the "synthetic" food was 12.2 gm.; during the four days of the "synthetic" period it was 10.9 gm. In Case 2 the intake in the ante-

cedent period averaged 6.9 gm.; during the "synthetic" period it averaged 7.1 gm. In Case 3 the average intake for eighteen days before the "synthetic" period was 9.03 gm.; for the five days of the "synthetic" period it averaged 9.50 gm.

It would appear, therefore, that the total salt intake could not be regarded as a factor in producing the fever. That the sodium hydrate added was of itself sufficient to cause a rise in temperature seemed most improbable. One observation was made, however, which bears on this point. Since sodium hydroxid was used to neutralize the phosphoric acid of the casein, sodium phosphate was added to a diet which had caused no fever (fat, 2 per cent.; sugar, 6.5 per cent.; protein, 2.6 per cent.); this was continued for four days without result so far as fever was concerned.

Inasmuch as the "synthetic" food was low in sugar (about 2 per cent.), although not lower than the food used in the period immediately preceding it, one observation was made on Case 3 during the febrile period to determine whether the addition of lactose to make the proportion in the food 5 per cent. would affect the fever. This was continued for two days without result. But two days later the fever ceased, twenty-four hours after the food had been changed.

We come now to a consideration of the amount of whey in the "synthetic" food formula as compared with that used in the other food formulas containing high protein. The latter were prepared (*vide* Miss Courtney's paper, Part IV) after the manner of Finkelstein's *Eiweissmilch*. In 1,500 c.c. of this food which were prepared for one day, there were used 600 c.c. of milk; while in the "synthetic" formula but 200 c.c. of milk. It will be remembered that no child took over 1,260 c.c. daily, and therefore the whey received was less than 175 c.c. It seems to us that the most probable explanation of the fever observed in these infants is the administration of the large amounts of protein without a sufficient amount of whey.

As to the actual significance of the retention of the chlorids, we have at present no definite information. It is, however, noteworthy that the chlorid intake in the "synthetic" food averaged about 0.50 gm., while that on the other foods was nearly three times as great; but such a reduction of the chlorids in normal infants did not bring about a complete disappearance of the chlorids from the urine.

CONCLUSIONS

1. Alimentary fever may under certain conditions occur in infants after administration of casein of cow's milk and perhaps of other proteins.

2. The rise of the body temperature was observed only when the food mixture was made up so as to contain about 6 per cent. of protein (chiefly casein) and a minimal quantity, only about 150 to 175 cc. of milk daily.

3. The rise of body temperature was invariably accompanied by a retention of chlorids, which, however, usually preceded the febrile attack by two or three days.

4. After the first rise of temperature the fever persisted so long as the diet was continued, but in every instance promptly disappeared as soon as the food was changed.

5. The fever is apparently due to the direct action of the absorbed protein, since the bacterial conditions of the intestines noted during the period of the "synthetic" food were not different from those noted during the preceding period. Also, Conclusion 4 speaks in support of this view.

6. From the observations here reported it would appear that the changes in the food influenced the chemistry of the excreta more than they did the bacteriology. For while the chemical changes resulting from the food variations differed considerably in the individual cases, the bacteriology changed along the same general lines in all. In view of this fact and of the slow changes in the intestinal flora noted in these observations, such changes would seem to have but a limited application for therapeutic purposes, though a very definite one when the food changes can be made sufficiently great.

7. It seems clear from these observations that one may use considerably higher percentages of protein in milk formulas than the 3.5 per cent. of Finkelstein's formula. This is a point which may be of much practical importance in conditions in which there is marked intolerance both of fats and carbohydrates. Such high proteins as 4.5 per cent. or over should only be used for limited periods, and never given at all except with a suitable proportion of whey.

8. This report emphasizes the physiologic importance of whey in the nutrition of infants and other young animals. While laying stress on the dangers of whey, especially from its sugar content, in many forms of intestinal disturbance, Finkelstein and Meyer have also appreciated the dangers to nutrition which may follow reduction of the salts. Recently Osborne and Mendel³ also have found that the mineral salts in the proportion present in whey were absolutely essential for the growth of animals, and that in the absence of salts, though maintenance of life was possible, growth could not be induced. As yet it is not possible to

3. Osborne, T. B., and Mendel, L. B.: *Carnegie Inst. of Washington*, Pub. 156, 1911, i and ii.

formulate any definite opinion as to the nature of the whey components which inhibit that action of casein, which, in the absence of whey, causes the rise of body temperature.

9. The present observations call special attention to the work of V. C. Vaughan⁴ and his collaborators, who have repeatedly reported the production of fever by the subcutaneous injection of various proteins. Whether or not the fever induced clinically in our cases and experimentally by Vaughan is occasioned by the same mechanism, remains to be established.

PART II.—CLINICAL OBSERVATIONS

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CASE 1.—Francis H. was admitted as a case of marasmus July 11, 1911, aged 8 months, having suffered from digestive disturbances, chiefly intestinal, since 3 months of age. At the time of admission he weighed but 3,850 gm., had no acute symptoms, but was suffering from chronic otitis and was very backward in physical development. During the next two months his digestion and general condition slowly improved. There was an initial loss in weight of 350 gm. till July 24, when he touched his lowest point, 3,500 gm.; from this time there was a steady but slow increase in weight amounting to over 800 gm., and he was taking a formula made from whole milk, containing fat, 2.6 per cent.; sugar, 5 per cent.; protein, 2.4 per cent.; 180 c.c. for each of seven feedings. His stools for the most part were good; no acute symptoms were present.

Metabolism observations were begun on September 14, at which time his weight was 4,330 gm. His appetite was excellent, there was no vomiting and his stools were 3 to 4 daily, usually yellow in color and seldom contained mucus. No change in food was made for two weeks. He continued to gain in weight, his stools were for the most part yellow and smooth, but at times became thin and loose. The number greatly increased while in the metabolism bed; there were eight to eleven daily, but most of them were small. The temperature remained normal and the child was comfortable and happy.

On October 1 the food was changed to a formula consisting of fat, 2.6 per cent.; sugar, 3.0 per cent.; protein, 2.4 per cent. The reduction in sugar was made on account of the rather frequent, thin stools. This food was continued for three weeks. The stools were less frequent but still somewhat thinner than normal and yellow, averaging from seven to nine daily. The child was kept in the metabolism bed, except for an interval of two days, the weight up to this time being about stationary.

October 14 the food was changed to fat, 0. per cent.; sugar, 6 per cent.; protein, 3.5 per cent. This was fat-free cow's milk with the addition of 1.5 per cent. cane sugar. This food was continued for five days, during which time he gained 250 gm. in weight and seemed perfectly comfortable. The stools showed, however, a marked and immediate change; they became large, loose and contained quantities of greenish-brown jelly-like mucus; there were from eleven to thirteen daily.

October 19 the food was made fat, 1.6 per cent.; sugar, 4.7 per cent.; protein, 3 per cent. This formula was obtained from partially skimmed milk with the

4. Vaughan, V. C., Cumming, J. G., and Wright, J. H.: *Ztschr. f. Immunitätsforsch.*, 1911, ix, 458; Vaughan, Cumming, and McGlumphy, C. B.: *ibid.*, 1911, ix, 16.

addition of .75 per cent. of cane sugar. This was continued for five days. With this change the amount of mucus somewhat diminished, the stools were reduced to eight a day and they were not so thin. The child lost during the five days about 100 gm. in weight.

October 25 he was given casein milk (*Einweissmilch*), three parts, and barley-water, one part, the formula being fat, 1.9 per cent.; sugar, 2.3 per cent.; protein, 2.9 per cent. The effect of the reduction in the sugar was immediate and very striking. The stools became smooth, soft, brown, formed, from three to four a day, and the amount of water in the stools which had been from 100 to 300 c.c. daily was reduced to 36 to 43 c.c. a day.

October 31 his food was changed to a formula consisting of fat, 3.6 per cent.; sugar, 3.1 per cent.; protein, 5.6 per cent. This was continued for one week; during this time the stools were gray, yellow, dry and formed, from four to five daily. He more than regained his lost weight, having reached 4,980 gm. His first metabolism period closed November 6.

During the interval between November 6 and 16 he was out of the metabolism bed and was being fed casein milk of the following percentages: fat, 2.75; sugar, 1.8; protein, 3.9. The weight remained stationary and the stools averaged three to four a day, being yellow, pasty and at times formed.

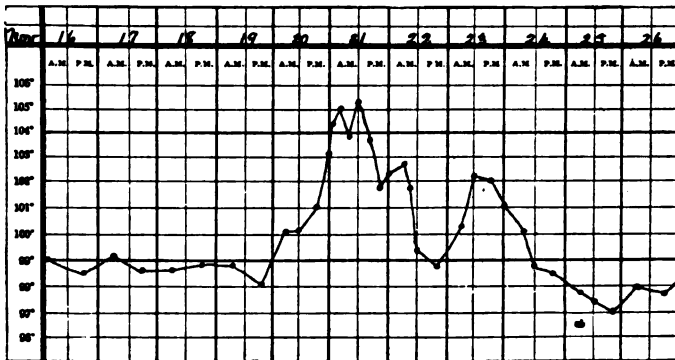


Chart 1.—Temperature of F. H.; first attack of fever.

November 16 he was again put in the metabolism bed and the food was changed to the following: fat, 2.9 per cent.; sugar, 1.5 per cent.; protein, 5.8 per cent.; this is referred to in the chemical report as the "synthetic" food. Up to this time the general condition of the patient was excellent; he was happy, comfortable and did not appear to be disturbed by the restraint of the metabolism bed. For the first four days he took his food well. The character of the stools, on this new food, changed considerably. They became gray, formed, dry and crumbly, occasionally being coated with mucus. The frequency remained about the same, three to four daily. On the nineteenth he refused 120 c.c. of the 1,260 c.c. offered, but showed no other signs of disturbance. On the morning of the twentieth the temperature was 100.2 F.; he vomited once and took less than half of his usual food. He was restless, fretful, irritable, and had a slight cough and a few coarse rales in the chest. His slight bronchitis was thought sufficient to explain his symptoms. The course of his temperature is shown on the accompanying chart (Chart 1). In the early morning of the twenty-first it was 106.2 F.; the child was pale, considerably prostrated, breathing rapidly, restless and continually rolling his head from side to side. His symptoms suggested the beginning of a pneumonia, although the only signs in the chest were a few rales. The suspicion was strengthened on examination of the blood which showed a leukocytosis of 27,160. Further evidence was shown by examination of the urine which showed a total absence of chlorids.

CASE 2.—Jacob S. was admitted Dec. 11, 1911, aged 5 months; suffering from malnutrition; weight 3,437 gm. The patient had gained little since birth, his digestive symptoms being chronic constipation and frequent vomiting. For the first two and one-half months in the hospital he was fed chiefly on dilutions of whole milk, with small amounts of maltose added. His digestive symptoms steadily improved. His stools averaged two to three a day, usually smooth and pasty, and he gained 551 gm. in weight.

February 27 he was put up in the metabolism bed and given a milk mixture whose formula was fat, 1.45 per cent.; sugar, 5 per cent.; protein, 3.5 per cent. He was given 150 c.c. for each of seven feedings, with 15 c.c. of olive oil every day. Two days later the protein percentage was increased and the sugar decreased, the formula being: fat, 1.45 per cent.; sugar, 4.5 per cent.; protein, 4.0 per cent. The percentage of protein was gradually raised and that of the sugar lowered at three day intervals until on March 13 he was taking fat, 1.45 per cent.; sugar, 2.1 per cent.; protein, 6 per cent., made after the manner of casein milk. On March 11 the olive oil was reduced to 6 c.c. and 5 per cent. lime water was added on account of occasional vomiting.

March 18 the food was changed to the "synthetic" food: fat, 1.45 per cent.; sugar, 1.8 per cent.; protein, 6 per cent. Up to this point he had done extremely well; had gained 501 gm. in weight and averaged three to four stools daily, which were for the most part yellow, pasty, but small, and inclined to constipation. He

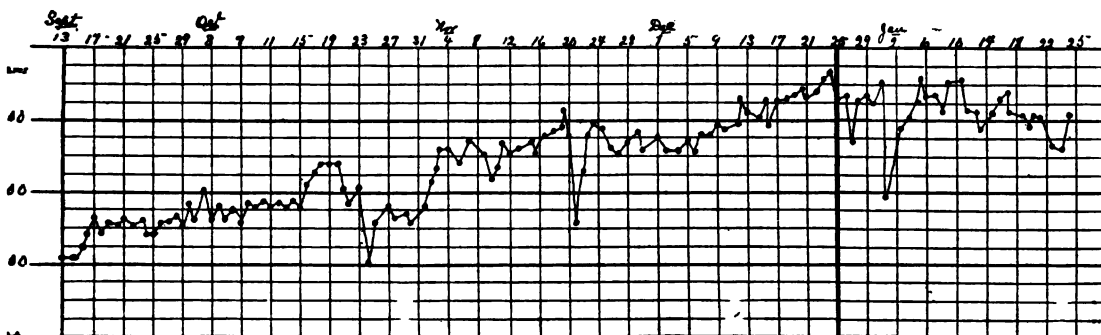


Chart 3.—Daily weight chart of F. H.

manifested no unusual symptoms and appeared in every way normal. After taking this food well for three days he showed his first sign of disturbance, which was to refuse some of his food. At noon of the following day (twenty-first) the temperature rose to 99.4 F.; at 7 p. m. it was 103.2 F.; it fluctuated irregularly for the next week, usually being between 100 and 102 F. During this period (up to March 27) his food was unchanged but he took it badly, frequently leaving more than one-half of the amount offered. The stools averaged three to six a day; they were small, of a yellow-brown color, often dry, hard balls, quite different from those of Case 1 on the same food.

It was thought that his constipation might be the explanation of his temperature. He was given two drachms of castor oil, and later calomel. The stools following catharsis were loose and contained considerable mucus, but the temperature continued. Careful and repeated physical examinations revealed no local cause for his temperature. He had few symptoms except a moderate amount of irritability, marked anorexia and a rapid loss in weight.

Beginning March 25, 30 c.c. breast milk were given before each feeding. This produced no change in the symptoms and finally on March 27 the "synthetic" food was stopped; whereupon the temperature rapidly fell to normal and remained so, except for one slight rise several days later, due to antitoxin. He rapidly regained his appetite and in three or four days was gaining steadily in weight.

The blood-examinations made are given in a subsequent table.

The patient was discharged from the hospital six weeks later in good general condition, weighing 4,471 gm.

For daily weight record during the period of observation see Chart 5.

CASE 3.—F. D. was admitted September 14, 1911, aged 4 months, suffering from chronic indigestion, weight 3,045 gm. From this date, except for one slight upset in December, his digestion and general condition improved; he took his food



Chart 4.—Temperature of J. S.

well, vomited but seldom, and his stools averaged three to four a day, were brown, pasty, at times somewhat constipated. His feedings consisted for the most part of dilutions of whole milk; his best weight, in December, showed a gain of 1,230 gm.

January 5 he was put in the metabolism bed and given a food consisting of fat, 1.5 per cent.; sugar, 2.2 per cent.; protein, 3.4 per cent. The protein was

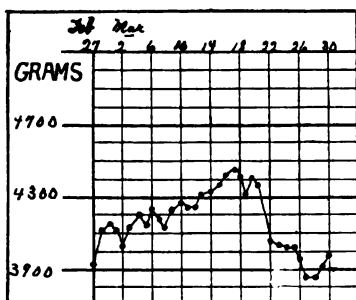


Chart 5

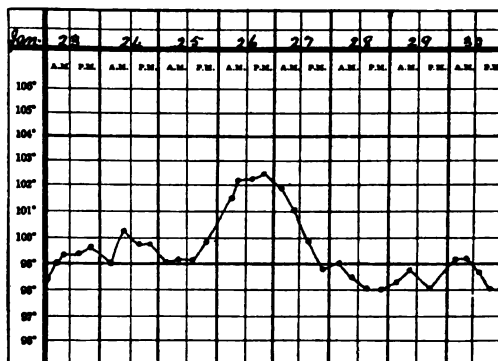


Chart 6

Chart 5.—Daily weight chart of J. S.

Chart 6.—Temperature of F. D.; first attack of fever.

gradually increased at three day intervals to 6 per cent. on January 18. He gained 164 gm., was happy and comfortable and his stools averaged six to seven a day, usually gray and pasty, rarely loose.

January 22, he was given the "synthetic" food: fat, 1.8 per cent.; sugar, 1.8 per cent.; protein, 5.9 per cent. On the evening of January 25 his temperature rose to 99.8 F. and in the morning of the following day to 101.6 F. The fever

was accompanied by irritability, restlessness, rapid breathing, and considerable prostration. He was immediately removed from the metabolism bed, given a cathartic and the food changed to a formula made from whole milk containing of fat, 1.5 per cent.; sugar, 5 per cent.; protein, 1.4 per cent. These measures were followed by an almost immediate change for the better. The loss in weight of 180 gm. was quickly regained and he continued to improve till his discharge on March 5, when his general condition was excellent.

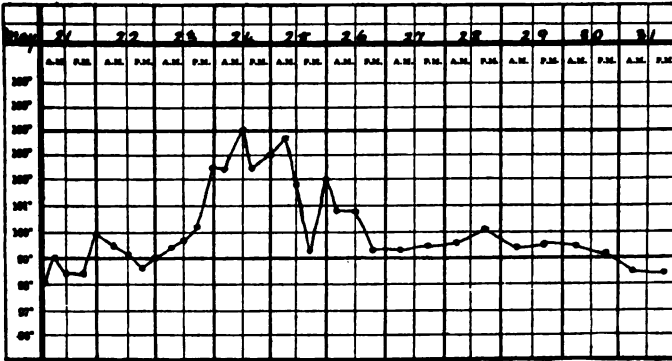


Chart 7.—Temperature of F. D.; second attack of fever.

March 10 the patient was readmitted with symptoms similar to those with which he first entered the hospital. For the following six weeks his digestion and general condition improved and he gained 720 gm. For the most part his food consisted of various dilutions of whole milk with sugar added and his stools were good.

On May 1 he was put in the metabolism bed, his food being: 2.6 per cent. fat, 4.5 per cent. sugar, 5 per cent. protein, and in addition was given 7.5 c.c. of olive oil each day. The protein in his milk was increased to 6 per cent. on May 4 and then kept at this point. During the interval between May 1 and 20 he gained 350 gm. His stools averaged two to three a day, mostly yellow and pasty, at times dry and constipated, requiring an occasional dose of magnesia. In his general condition he improved steadily.

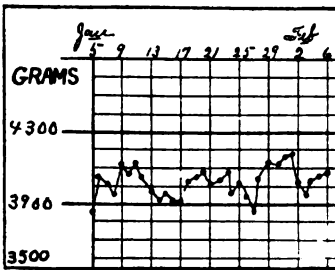


Chart 8

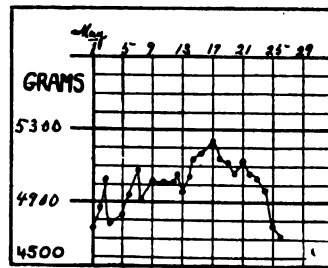


Chart 9

Charts 8 and 9.—Daily weight charts of F. D.

On May 20 he was put on the "synthetic" food; except for the existence of constipation nothing noteworthy happened until the evening of May 23 when the temperature rose to 101.8 F., but no other manifestations occurred till the afternoon of May 24, when he was noticed to be restless, refused part of his food and vomited once. On May 24 lactose to 5 per cent. was added to the "synthetic" formula but with no apparent effect on the symptoms. On the morning of May

25 the symptoms practically identical with those observed on previous similar occasions with other children developed, but of greater severity. He was immediately removed from the metabolism bed, given a cathartic and the food changed to a dilution of whole milk. With these measures all the symptoms speedily disappeared and in thirty-six hours he was apparently as well as ever.

He was discharged June 27 in good general condition, having gained 1,740 gm. since March 20.

In Table 1 are given the results of the various blood-examinations made in the different cases.

TABLE 1.—RESULTS OF BLOOD-EXAMINATIONS IN THE THREE CASES

Case	Period	Condition	Total Number Leukocytes	Polymorpho- nuclears, Per cent.	Lymphocytes, Per cent.	Remarks
F. H.	Nov 21..	First day of fever	27,160	57.6	37.0
	Nov. 25..	First day of normal T.	9,240	37.3	54.0
	Dec. 30..	Normal temperature	20,200	46.0	49.0	Slight otitis present
	Dec. 31..	Fever beginning	17,900	42.0	52.0
	Jan. 1..	Fever high	17,400	49.5	41.5
	Jan. 2..	No fever	18,200	46.0	45.3
	Jan. 3..	No fever	14,200	39.2	49.5
	Jan. 4..	No fever	13,800	43.0	47.0
	Jan. 5 to 8.	No fever	16,400	47.3	46.9	Average for four days
J. S.	March 13..	No fever	18,400	42.0	51.5
	March 16..	No fever	18,800	51.0	49.0
	March 20..	No fever	19,800
	March 21..	Fever began
	March 23..	Fever present	14,400	57.0	43.0
	March 24..	Fever present	16,400	42.0	57.0
F. D.	Jan. 22-25..	No fever	8,700	Average for four days
	Jan. 26..	Fever began	10,700
	Jan. 27..	Fever present	14,300
	Jan. 28..	No fever	10,000
	Jan. 29..	No fever	8,300
	May 21-23..	No fever	15,600	54.3	42.0	Average for three days
	May 24..	Fever high	20,000	50.0	50.0
	May 25..	Fever high	20,000	46.0	54.0
	May 26..	Fever slight	18,200	44.6	55.0
	May 27..	No fever	12,800	42.0	58.0
	May 29..	No fever	9,200	47.3	52.6

Case 1 in the first period with high temperature showed marked polymorphonuclear leukocytosis,⁵ which quickly disappeared when the temperature became normal. In the second period the variations during the fever from the average for the child were so slight as to be without significance.

5. It is to be borne in mind that in infants of this age and type the lymphocytes normally exceed in number the polymorphonuclear cells.

Case 2 showed no marked variations during the febrile period from the findings before and subsequent to it.

Case 3 showed a distinct leukocytosis coming with the fever and disappearing with it. In the second observation on this patient the same thing was seen, the differential count being inconclusive.

SUMMARY

In every one of the five observations made on the three infants, an attack of fever followed the administration of the "synthetic" food, although in all the temperature had been previously normal for a considerable period. Three times this developed on the fourth day, once on the fifth and once on the sixth day. In four observations the patients had previously taken as high, or nearly as high, a percentage of protein in food prepared differently for much longer periods (in one case for sixteen days) without the development of fever. In every instance the fever developed abruptly without other warning than anorexia and some restlessness which usually preceded the rise of temperature for about twelve hours. The fever persisted so long as the diet was continued, but ceased almost at once when the food was changed to a simple milk dilution. With the fall in temperature all of the general symptoms speedily disappeared.

The highest temperature noted was 105.4 F. In the patient showing the least reaction it rose to 102.5 F. The average rise was to 104 F. Marked nervous symptoms usually accompanied the fever; constant rolling of the head, extreme restlessness, pallor, rapid respiration, considerable prostration, and in three observations marked leukocytosis. In one case the white cell count reached 27,000. Digestive symptoms, except anorexia, were conspicuously absent. Initial vomiting was noted but once; the bowels were usually somewhat constipated but not otherwise abnormal; a moderate abdominal distention was noted but once; neither pain nor tenderness was evident in any case. The urine showed several times an increased indican reaction, but this was not constant nor persistent. Pallor, rapid respiration and prostration were marked in all but one case. In every instance there was rapid loss of weight, which was due partly to the refusal of food and partly to catharsis. This loss was soon repaired in nearly every case. In none of the observations did the symptoms resemble an ordinary attack of acute indigestion.

PART III.—BACTERIOLOGIC OBSERVATIONS

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Throughout these five periods of observation the method of procedure was the same. Specimens of feces obtained from the rectum were studied bacteriologically for several days before the chemical examination

of the excreta was begun. This served the purpose of establishing a control for each child. Throughout each period of study daily examinations of the feces were made.

TECHNIC

The samples of feces were obtained in the usual way, by introducing into the rectum a glass tube of narrow caliber, plugged at one end and sterilized. As a rule, the tube became filled with fecal matter within a few seconds, but during the periods of constipation it was difficult to obtain more than a small amount, sometimes less than half a cubic centimeter, in several minutes. Occasionally no material at all could be obtained even in more than one attempt. From the fecal specimens smears were prepared and stained by Gram's method, the remainder of the material being at once emulsified in neutral, dextrose-free broth. The emulsion was made as thorough as possible, and care was taken lest it be too thick. This emulsion served to inoculate glucose and lactose fermentation tubes, whole milk tubes and tubes of the acid-dextrose-broth introduced by Heymann, and described by Finkelstein⁶ as consisting of 2 per cent. dextrose in 0.5 to 1 per cent. acetic acid broth. Agar and gelatin plates were also poured from the tube of emulsified feces, which was then itself incubated and compared with the growths in the acid broth on the following day. The cultures were incubated both aerobically and anaerobically, but it was soon found that anaerobic cultivation of plates poured directly from the fecal emulsion was utterly useless, since the colon varieties overgrew all other forms. Anaerobic incubation was, therefore, reserved for the cultivation of second or later generations from the acid broth or fermentation tubes, and of colonies isolated from deep agar sticks and grown further on plates or in fluid media.

It may be said at the outset that the varieties of bacteria isolated from the stools of these three infants were not numerous. There was a marked sameness noted in the bacteriology throughout all the observations, a fact which was to be expected since the food was practically the same in the parallel stages of the five observations. While by no means every variety of bacterium seen in smears and cultures from the feces was isolated in pure growth, the great majority were certainly so obtained. The most useful media proved to be the lactose broth in the fermentation tubes, and the acid-dextrose broth or Heymann's medium. Gelatin plates were useful in giving a general idea of the varieties of liquefying organisms present. Whole milk tubes proved to be disappointing as indicators of the presence of proteolytic bacilli, for the reason that streptococci which peptonized milk were very numerous in the

6. Finkelstein, *Deutsch. med. Wchnschr.*, 1900, xxvi, 263.

feces of these children, and it was repeatedly noted that on a diet rich in carbohydrates, where the cultures showed the presence of a fermentative and not a proteolytic flora, the amount of gas in the fermentation tubes was comparatively low as was to be expected, but the milk tubes were more than 80 per cent. peptonized. As a control a breast-fed baby was studied. This child showed the typical bifidus picture in smears and cultures from the stool. Only 0.5 to 1 c.c. of gas was formed in the lactose fermentation tube, and yet the milk tubes were almost completely peptonized. The liquefying streptococcus was found in large numbers in the stool from this infant.

BACTERIOLOGY OF THE FOOD

In order to determine whether the bacteriologic intake with the food bore any relationship to the fecal flora, samples of the food were studied at intervals. At the beginning of the first observation, Sept. 13, 1911, the prepared food contained *Streptococcus*, *Albococcus*, *B. lactis aerogenes* and a liquefying, fluorescent bacillus. There were 12,000 colonies to 1 cubic centimeter of food. Nine days later the number of colonies had risen to 3,500,000 per c.c., and *B. subtilis* was isolated as well as the other varieties. It became obvious that a cleaner milk was needed, and a change was made on October 11. The number of colonies in the new milk used numbered only 1,600 to the cubic centimeter, and were composed only of staphylococci and streptococci. The food after it had been prepared for the feeding of the child, however, contained 16,000 to 19,000 colonies to the cubic centimeter, and on several successive days *Streptococcus*, *Aurococcus*, *Albococcus* and *B. coli communior* were found. Greater cleanliness in handling of the bottles was then instituted, and after November 1 no further contaminations appeared in the food. The protein milk contained the largest numbers of bacteria, 200,000 to the cubic centimeter being present on one occasion. This was reduced to 30,000 later. From the ripened milk used in preparing the protein milk a long gram-positive bacillus was isolated. It grew very faintly on agar, fermented lactose, and coagulated milk softly without peptonizing the curd to any extent. This bacillus was looked on as *B. Bulgaricus*, described as a powerful lactic acid ferment by Cohendy,⁷ and with which the milk was said to be ripened. Herter and Kendall⁸ found this bacillus in the feces of a rhesus monkey fed on *bacillac*.

The "synthetic" food never contained over 2,000 colonies to the cubic centimeter.

7. Cohendy, M.: Compt. rend. Soc. de biol., 1906, lx, 558.

8. Herter and Kendall: Jour. Biol. Chem., 1908-9, v, 293.

Five observations were made on three children. The details of the bacteriologic findings during the course of the studies follow:

Observation 1.—F. H., 9½ months old. Sept. 13, 1911. Food, modified milk having percentages of fat, 2.6; sugar, 5; protein, 2.4; containing albococci, streptococci, fluorescent bacilli which liquefy gelatin, and *B. lactis aerogenes*.

Feces yellow, no mucus present. The material was granular and did not make a smooth emulsion in dextrose-free broth. Smear shows oval cocci in pairs and chains, slender, gram-positive bacilli, some with pointed, tapering ends (*acidophilus*); granular or vacuolated bacilli, some with poles staining deeply; gram-negative bacilli like *B. coli* forming a background for the larger, blue, bacillary forms. No spores were seen.

From agar plates an oval streptococcus, the *Enterococcus*, and *B. coli communis* were isolated. In the fermentation tubes small numbers of *B. bifidus* grew, and were subcultured, though not isolated, in acid broth in the anaerobic jar (pyrogallic acid—hydrogen—vacuum method). *B. acidophilus* was isolated from the acid broth tube. Only 1.5 c.c. of gas formed in the fermentation tubes of lactose broth, and 1.25 c.c. in the glucose broth. Milk was coagulated and slightly peptonized.

September 16.—Three days later there were more blue than red bacteria noted in the gram-stained smear, and in the cultures *staphylococci*, *streptococci*, *B. acidophilus*, *B. bifidus*, *B. coli communis*, and *B. fluorescens* liquefying gelatin were noted. Only 1 to 1.5 c.c. of gas formed in the fermentation tubes, and whole milk was markedly peptonized, only a small solid coagulum remaining in the bottom of the tube. On gelatin plates liquefying green colonies and liquefying white colonies developed of fluorescent bacilli and albococci.

This picture varied but slightly during the following week, *B. coli communis* being found one day and a strain of the Shiga (non-mannite fermenting) type of *B. dysenteriae* another day. The history disclosed the fact that the child had suffered from "loose bowels" for a period of four weeks before admission, which was sought because of vomiting, diarrhea and colic.

September 23 *B. subtilis* was found in the feces. The colon bacilli were very numerous, but *B. bifidus* was present in comparatively smaller numbers. These relative proportions continued until the change to cleaner milk October 11, four days after which date no more *subtilis* bacilli were noted.

October 15: Food, milk with percentages, fat, 0; sugar, 6; protein, 3.50.

October 16. Cocci and colon bacilli were very numerous; *B. acidophilus* was present and *B. bifidus* had increased in numbers. *B. lactis aerogenes* was also found. The amount of gas produced was small and milk was coagulated but only very slightly peptonized.

October 19. Food changed to fat, 1.6; sugar, 4.5; protein, 3.

The numbers of *B. coli* were very numerous, *B. communior* being found on several successive days. *Staphylococci*, *diplococci* and *streptococci* were present in very large numbers.

October 20. *B. perfringens* (*B. aerogenes capsulatus*, Welch) was noted.

October 23. A fluorescent, liquefying bacillus was found on gelatin plates.

October 24. Food changed to protein milk, diluted with barley water: fat, 1.9; sugar, 2.3; protein, 2.9, but the child refused it for twenty-four hours.

October 25. A specimen was obtained after the child had fasted one whole day. The smear showed an equal number of gram-negative and gram-positive bacteria, having hitherto always shown more of the Gram-positive type. The change was due to the small numbers of cocci present, while colon-like bacilli were numerous and some gram-positive bacilli, apparently *B. aerogenes capsulatus*, were seen. The amount of gas in the fermentation tubes was more than twice as great as it had ever been, and in them *B. aerogenes capsulatus* was growing together with colon bacilli and cocci.

October 26. A long gram-positive bacillus was present in addition to the other varieties. This bacillus was apparently identical with the *B. bulgaricus* in the food, which was made up with ripened milk.

The only change noted in the next few days was a marked increase in the amount of gas found in the fermentation tubes, no new varieties of bacteria being noted.

October 31. Food changed to fat, 3.6; sugar, 3.1; protein, 5.5.

The amount of gas grew larger, the cocci decreased in numbers while colon bacilli and gas bacilli were numerous. There were very few bifidus forms seen.

November 6. Food of the same formula, but three drachms of maltose were added to relieve the constipation. From the dry maltose a large, gram-positive spore-bearing bacillus identified as *B. megatherium* was isolated. The day following the addition of the maltose to the food this spore-bearing bacillus was present in the feces. Castor-oil was given.

November 8. Cocci were very numerous; many colon bacilli and large spore-bearing, gram-positive bacilli were also seen. The spores in some of these bacilli were oval in shape, situated in the center of the organism, giving the whole bacillus an oval form; while in others a round spore lay at one end, giving the bacillus a nail-shape; in still others the spore was situated in the center of the bacillus and was narrower than the body of the rod, thus not changing its shape. Two forms of spore-bearing bacilli were isolated and identified as *B. mesentericus* and *B. megatherium*. Both peptonized milk without forming acid, both fermented dextrose and saccharose, *B. mesentericus* fermenting mannite as well. *B. bulgaricus* was still present.

November 10. The food was changed to fat, 3.1; sugar, 3.4; protein, 3.9, with the addition of four drachms of maltose.

November 12. The feces were alkaline to litmus paper. The suspension of feces in dextrose-free broth incubated twenty-four hours gave a very deep indol reaction. Milk tubes were coagulated and almost completely peptonized. Much gas formed in the fermentation tubes. Cocci were numerous, as were colon bacilli and *B. mesentericus* with many oval spores. *B. bulgaricus* was not found, though ripened milk was still used in the food.

November 16. The food was changed to the "synthetic" mixture, fat, 2.9; sugar, 1.5; protein, 5.8.

November 18. Cocci and colon bacilli were numerous. The feces were alkaline to litmus and a twenty-four hour culture in dextrose-free broth gave a deep indol reaction. The most numerous variety of organism present was a gram-positive bacillus isolated as *B. mesentericus*. On gelatin plates many slowly liquefying colonies developed.

November 20. In the smears there were many spore-bearing gram-positive bacilli on a background of colon-like gram-negative bacilli; some cocci; some gram-positive bacilli without spores. In the fermentation tubes the gas was reduced to half the quantity of the previous days, and in the one containing lactose broth some acidophilus and very many bifidus bacilli grew together with *B. mesentericus* and cocci.

November 21. After a sharp rise in temperature and the development of some prostration, a laxative was given and the food changed to barley water for a day. The laxative brought away large numbers of the organisms present the day before, and more *B. acidophilus* and *B. bifidus*, and, in addition, *B. aerogenes capsulatus*.

During the next week the child was fed only diluted milk, varying from fat, 1.2; sugar, 5; protein, 1, to fat, 2.20; sugar, 5; protein, 1.75. The spore-bearing bacilli diminished in number but did not disappear entirely. *B. bifidus* remained in small numbers, and so did *B. aerogenes capsulatus*. Within another week, during which time the sugar in the food was kept at 4.50 per cent., *B. acidophilus* and *B. bifidus* had increased in number, and only an occasional spore-bearing bacillus was seen. The amount of gas diminished, and the milk-tubes were about half peptonized. The second observation was then begun on the same child.

Observation 2.—F. H., now 1 year old, Dec. 12, 1912. Food: Fat, 2; sugar, 5.7; protein, 2.6. Maltose in food. The cocci and the colon bacilli were numerous, but *B. acidophilus* and *B. aerogenes capsulatus* were more so. *B. megatherium* appeared in forty-eight hours (from the maltose). The amount of gas varied, but was rather large, and milk was almost completely peptonized.

December 26. "Synthetic" food begun: fat, 2.1; sugar, 1.7; protein, 6.3. During the next four days *B. mesentericus* appeared in large numbers, while *B. aerogenes* disappeared. The gelatin plates were rapidly liquefied. *B. acidophilus* was less numerous, *B. coli* more so.

December 30. Fever and prostration developed. Castor-oil was given, after which *B. bifidus* reappeared and increased markedly during the next four days, the food in that time being the milk formulas 1-5-90 and 2.60-5-2.40.

Jan. 4, 1912. Cocci, colon bacilli, *B. acidophilus*, *B. bifidus*, and an occasional *B. mesentericus*.

It will be noted that the changes in the intestinal flora throughout these two observations was a very gradual one, consisting of a diminution but not a complete disappearance of the normal fermentative flora and its replacement by some proteolytic varieties. While the relative differences in the proportions of the amount of protein and carbohydrates in the food were as wide as it is possible to make them in the feeding of an infant of this age, it nevertheless follows that as long as the diet remains one composed entirely of milk elements, the absolute proportions cannot be changed to such a degree as to alter the flora completely. Thus the slow and incomplete change is accounted for. Compared with the results of the experiments of Herter and Kendall⁹ on kittens and monkeys, where the protein diet of meat and eggs was changed to one of milk plus dextrose, the difference is certainly a striking one. The presence of *B. acidophilus* at a time when the reaction of the feces was neither amphoteric nor alkaline to litmus, may be accounted for by the fact that this acid-loving bacillus really grows better in a slightly alkaline medium, a fact pointed out by Rodella.⁹ Certainly *B. bifidus* branches very much more in acid than it does in alkaline media, which accounts for the straight forms seen in the stained smears from these stools, and proved to be *B. bifidus* by culture in the fermentation tubes containing sugar broth. It will also be observed that after the catharsis and a return to a diluted milk formula at the end of the periods of study, the child's intestinal flora was about the same as it had been at the beginning. The return to normal was practically accomplished in from seven to ten days.

Observation 3.—F. D., aged 4 months, Jan. 1, 1912. Food, milk with following percentages: fat, 2.40; sugar, .50; protein, 2.20. Gram-stained preparations showed the presence of cocci in pairs and chains, few colon-like bacilli and *B. acidophilus*. In cultures all these and *B. bifidus* appeared. Two days later *B. megatherium*, from the maltose used in the food, appeared in the feces. After a change to food made with ripened milk (1.7-2.20-3.5) *B. bulgaricus* was seen.

9. Rodella, A.: Centralbl. f. Bakteriol., 1901, xxix, 717.

With an increase of the protein in the food to 4.7 per cent. spore-bearing *B. mesentericus* appeared and the colon bacilli were numerous. *B. bifidus* was present in small numbers only. Gas production in the fermentation tubes was very marked, milk-tubes were peptonized and many liquefying colonies grew on gelatin plates. The "synthetic" food (2-1.50-6) was begun on January 22, and on the following day the colon forms were very numerous, but spore-bearing bacilli, together with acidophilus and bifidus gave the smear a gram-positive appearance. The spores were of a variety of shapes. Some were oval with only a small cap of bacillus body left at either end; some were round and placed at one end of the bacillus, giving an appearance similar to that of the tetanus bacillus, and some were of the same diameter as the bacillus body, in which they lay nearer one end than the other. Still both acidophilus and bifidus continued to grow until the rise of temperature and accompanying prostration on January 26. Many of the bifidus bacilli were vacuolated, and the *B. mesentericus* showed many gram-negative, evidently degenerated elements. On February 2 the picture was practically as it had been at the beginning of the study, but a few oval spore-bearing bacilli still remained. There was in general very little difference between this observation and the preceding ones.

Observation 4.—J. S., aged 7½ months. Food, milk with following percentage: fat, 1.45, sugar, 5; protein, 3.50. Feb. 27, 1912.

The preliminary examination of this child's rectal contents showed the presence of cocci in pairs and chains, comparatively few colon bacilli, some acidophilus and straight forms of bifidus, and very few spore-bearing bacilli probably taken in with the maltose added to the food. The picture was distinctly a gram-positive one. On the above food only a small amount of gas formed in the fermentation tubes, except on one day when, for no apparent reason, the gas formation was more than doubled and the comparative numbers of colon bacilli were greatly increased. Evidently peristalsis had brought down those bacilli from the region of the ileocecal valve just before the specimen was obtained for that day's observation. *B. bulgaricus* in small numbers appeared in the feces, but the cocci were by far the most numerous forms in both smears and cultures.

There was no appreciable change in the bacteria until the protein in the food reached 6 per cent. with 2.5 per cent. of sugar, when spore-bearing, gram-positive bacilli began to appear and *B. bulgaricus* was no longer found.

On this high protein food the floral changes proceeded slowly, cocci still remaining very numerous, colon bacilli gradually increasing in numbers, spore-bearing gram-positive bacilli increasing very slowly, and a few vacuolated forms of *B. bifidus* persisting.

March 18 the "synthetic food" began, fat, 2.1; sugar, 1.7; protein, 6.3, after which, although there were many free spores as well as those contained in both gram-positive and gram-negative bacilli, the numbers of acidophilus and bifidus bacilli were still so numerous as to grow without difficulty in lactose broth fermentation tubes and from them in deep stick lactose agar. After the febrile attack and the subsequent catharsis human milk was added to the infant's food. Within two days *B. bifidus* had appreciably increased in numbers, although *B. mesentericus* and spores were still present. On the third day *B. acidophilus* was isolated from the rectal contents. The return to a normal intestinal flora was more rapid in this child than in the other two. Whether the comparatively small amount of human milk (11 ounces) given him helped this event, or whether it was only a coincidence in a rather resistant baby, it is difficult to say without a repetition of the observation. It is suggestive, however, and agrees with Moro's¹⁰ experience, that when human milk is given to an artificially-fed baby, the physiologic flora appears in the stools on the second or third day.

10. Moro, E.: Jahrb. f. Kinderh., 1905, lxi, 687.

Observation 5.—F. D., now 8 months old; same child as in Observation 3.

A preliminary study of specimens of the rectal contents showed the presence of cocci, colon bacilli, *B. acidophilus*, *B. aerogenes capsulatus*, and a few gram-positive bacilli containing oval spores.

May 1, 1912. Food: fat, 2.6; sugar, 4.5; protein, 5.0. Within three days the formula was changed to fat, 2.6; sugar, 2.5; protein, 6, and the gram-stained slides prepared from the fecal material showed a very mixed picture. There were gram-positive cocci, very long gram-positive bacilli, some vacuolated gram-positive bacilli in parallel pairs or in small groups, large gram-positive bacilli containing spores, small ovals containing spores, gram-negative bacilli like the colon varieties, large gram-negative, granular bacilli, and some gram-negative bacilli containing spores. The amount of gas found in the fermentation tubes was very small, the milk tubes were coagulated but only very slightly peptonized. During the following week the picture remained the same, the bacteria cultivated from the feces including streptococci, staphylococci, *B. coli communis*, *B. bulgaricus*, and *B. mesentericus*. *B. bifidus* grew in the fermentation tubes. The only change observed during the following week was a decided increase in the amount of peptonization in the milk and gelatin cultures inoculated from the feces, and, in the smears, the number of spore-bearing bacilli increased comparatively, though all the other forms remained.

May 20. "Synthetic" food, fat, 2.06; sugar, 1.8; protein, 6. For two days there was practically no change distinguishable. At the end of that time, although the reaction of his rectal contents remained distinctly acid to litmus paper, the spore-bearing bacilli increased somewhat in numbers, *B. bulgaricus* had disappeared, the colon bacilli were less numerous, and bifidus forms were very few.

May 23. On the third day a rise in temperature occurred and the carbohydrate content of the food was increased to 5 per cent. the following morning, the protein remaining at 6 per cent. The spore-bearing gram-positive bacilli, isolated as *B. mesentericus*, still dominated the picture, bifidus forms also being present. As the temperature continued high, castor-oil was administered on May 25.

For a period of twenty days this child was fed on a mixture made with ripened milk, and *B. bulgaricus* was present in his rectal contents throughout that time. In one of the other studies (Observation 1) the period in which ripened milk was used in the food lasted twenty-three days, and in Observation 4 it lasted eighteen days. In neither of these cases, however, did the acid reaction of the rectal contents continue until the appearance of the fever, nor did *B. bulgaricus* appear in the feces throughout the entire period of feeding with ripened milk. This prolonged period of acidity did seem to delay the increase of proteolytic bacteria, though it did not entirely prevent their development. It would also seem that since all the clinical symptoms accompanying the end of this observation were as marked as they had been in the other four, the proteolytic bacteria were not the cause of those symptoms, but only the inevitable result of a comparatively high protein content in the food, and not, in themselves, harmful.

The slow increase of the proteolytes and the persistence of *B. bifidus* would seem to exemplify the statement of Tissier¹¹ that the rôle of *B. bifidus* is to keep the intestinal tube acid enough to arrest the development of many abnormal invaders, and to remove the proteoses necessary

11. Tissier, H.: Ann. de l'inst. Pasteur, 1905, xix, 119 and 272.

for the development of the latter. The presence of *B. bulgaricus* helped to increase the acidity, but even the combined acidity of the two was insufficient to prevent *B. mesentericus*, which attacks all proteins, from developing.

SUMMARY

To sum up the results of these five observations, we find that the varieties of bacteria identified as present in the rectal contents of the five children before and during the period of study included the following: *Albococcus*, *Micrococcus ovalis* or *Enterococcus*, a streptococcus proteolyzing milk, a streptococcus not proteolyzing milk, *B. coli communis*; *B. coli communior*; *B. lactis aerogenes*; *B. acidophilus*; *B. bifidus*; *B. bulgaricus*; *B. fluorescens*, liquefying gelatin. *B. dysenteriae* (Shiga) was found in one case.

During the periods of high carbohydrate in the food the cocci, colon bacilli, acidophilus and bifidus bacilli were most numerous; sometimes *B. aerogenes capsulatus* appeared.

During the periods of high protein content in the food, *B. mesentericus* gained the ascendancy, *B. aerogenes capsulatus* sometimes persisted, and the colon bacilli were increased in numbers. But the acidophilus and bifidus bacilli did not entirely disappear, probably because the change in the food was not complete nor prolonged enough.

Bacteria introduced with the food (*B. fluorescens*, *B. bulgaricus*, *B. subtilis*, *B. megatherium*) were found in the feces within a period varying from twenty-four to seventy-two hours.

The transition in the flora from one period to another was always gradual, never abrupt, recognizable changes requiring forty-eight to seventy-two hours to develop.

The return to the bacterial picture present at the beginning of the observation, which may be assumed to be the normal for that particular infant, was accomplished in from seven to ten days after the end of the study and subsequent catharsis.

As regards the children studied a second time, neither one gave any evidence of a more rapid reaction during the second observation than he had shown during the first.

PART IV.—OBSERVATIONS ON METABOLISM

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METHODS OF ANALYSIS

The methods used were mainly those described in preceding papers.¹² A few changes and additions are to be noted. In the determination of feces fat, a third portion of dried material was mixed with an excess of alcoholic solution of N/5

12. AM. JOUR. DIS. CHILD., 1911, i, 321-340; January, 1912, iii, 1-14.

sodic hydrate, thus binding the free fatty acids and leaving only neutral fat to be extracted. The values thus obtained for neutral fat are subtracted from those obtained from the simple extraction of the dried material, giving values for the free fatty acids present. Total ash was determined by heating in a platinum dish with small amounts of ammonium nitrate, cooling and weighing until weight is constant. For the determination of chlorid, the solid material was thoroughly mixed with dry sodium carbonate and charred, the alkali neutralized by nitric acid, the solution filtered off and titrated according to the Volhard method. Chlorids in the urine were also determined according to Volhard. The method for determining calcium has been described. Magnesium was determined in the filtrate remaining from the calcium determination by precipitating ammonium magnesium phosphate by addition of disodium phosphate, filtering through a Gooch crucible after an interval of several hours and heating the precipitate with a blast lamp until it is converted to magnesium pyrophosphate. Phosphates were determined in the urine by titration with uranium nitrate, potassium ferrocyanid being used as indicator.¹³ The solid material, dried milk and feces, was ashed to whiteness in a platinum crucible with powdered magnesium oxid, the residue dissolved in 10 c.c. hot 5 per cent. hydrochloric acid, neutralized to phenolphthalein with 5 per cent. sodic hydrate and 0.5 to 1 c.c. excess added, again neutralized by 10 per cent. acetic acid containing 10 per cent. sodium acetate and 2 to 3 c.c. more acetate solution added.¹³ The solution was then titrated with uranium nitrate as in case of urine.

PREPARATION OF FOOD MIXTURES

"Synthetic" Food Mixture.—A casein curd was obtained by allowing junket tablets to act on 4,000 c.c. of fat-free milk. The curd was drained through cheese cloth and washed four times with boiled water. A solution of the casein was effected in the following manner: The moist curd was ground in a mortar with successive small quantities of N/10 sodic hydrate and hot water until the mass resembled a thick boiled starch. (The alkali and water were sterilized by boiling.) A clear fluid solution of the casein was then effected by heating the paste for a few minutes in a double boiler. The solution of casein did not react alkaline, although it required 250 c.c. of sodic hydrate (1 gm. of the salt) to accomplish the solution. The final food mixture was made up by adding to the casein solution 200 c.c. of milk and the desired quantity of 32 per cent. cream. Boiled water was added to make up a volume of 1,500 c.c.; of these 1,260 c.c. were employed for feeding and the remaining 240 c.c. for analysis.

Other High Protein Food Mixtures.—The casein curd was prepared in the manner described in the preceding paragraph. The curd was then ground up and pressed through a fine sieve by the aid of 600 c.c. of ripened milk containing 2 per cent. fat. To this suspension boiled water, lactose, and 32 per cent. cream were added in desired proportion. The amount of fat-free milk employed for the curd, of lactose, and of cream varied for each feeding period in accordance with the desired formula; the quantity of ripened milk remained constant. The amount of protein in each mixture was calculated on the basis of average values obtained from the analysis of several samples of the curd obtained in the manner described in the preceding paragraph.

CASE 1.—Francis H. There were ten periods of observation beginning Sept. 14, 1911, and ending Jan. 1, 1912; each period represented a change in the food. During the first two he was on a normally-balanced diet the aim of which was to provide a standard for comparison with the other diets in which one of the constituents predominated, and the other two were given in a minimum quantity. The percentage composition of the food during the first period of nineteen days was 2.6 fat, 5.0 carbohydrate, and 2.4 protein; of the second standard period of twelve days, 2.6 fat, 3.0 carbohydrate, and 2.4 protein (*vide* Table 1). The daily calorific

13. Am. Vozárik, Ztschr. f. Phys. Chem., 1911-12, No. 76, v and vi, 426 and 433

intake of the food mixture of the first period contained 721 calories, and of the second period 690 calories. The general condition of the infant on this diet was fairly satisfactory. The average gain in weight was about 12 gm. per day in the first period, and about 5 gm. per day in the second period. The stools were very watery, contained some curds, were foamy, greenish and contained some mucus. The nitrogen balance was positive, reaching 1.2 gm. per day. The general composition of the urine indicated only a slight deviation from the normal in the first period, and scarcely any in the second period. The percentage of ammonia nitrogen in the urine was 8.5 of the total in the first period, indicating, perhaps, very slight acidosis. Creatin and creatinin output showed values differing little from those of the following periods. The ash retention in the first period was considerably higher than in the second, reaching the value of 2 gm. per day in the first, and 0.3 gm. in the second period. The stools presented a comparatively high total acidity, reaching in the first period the value of 903 and in the second period 779 per 100 gram of dried material.

In the third period lasting four days, and the fourth period lasting five days, the fat was removed from the food mixture in the third, and lowered to the proportion of 1.6 per cent. of the total food intake in the fourth period. The calorific intake was 567 calories in the third, and 649 calories in the fourth period. On this diet the appearance of the stools changed considerably. The color was copper-yellow, of watery appearance with considerable mucus, and with many hard curds. In the fourth period they gradually became granular, with many small fat curds, and the quantity of mucus then diminished. The general condition of the infant, as indicated by the body weight of the patient, was better in the third period than in the fourth, showing a gain of 25.7 gm. per day in the third, and a loss of 23.3 gm. per day in the fourth period. The nitrogen balance was positive in both periods, being 1 gm. per day in the third, and 0.7 gm. per day in the fourth. The composition of the urine in both periods indicates less acidosis than one noticed in the first two periods. Very striking were the fluctuations in creatin output; while the output of creatinin remained nearly constant.

This observation regarding creatin is rather in conflict with those made by Rose¹⁴ in Professor Mendel's laboratory and by Folin.¹⁵ It is not possible at the present moment to give an adequate explanation of the differences in the observations of Rose and of Folin on one hand and ours on the other. The considerable difference in the ages of the children may contain the reason for the discrepancy, or it may be occasioned by some accident of the observation.

The total mineral balance was less favorable during these two periods as compared with the first two. The chemical changes in the composition of the feces were not striking, the acid value per 100 grams being about the same as in the second period. As a significant distinction one may point out the proportion of soaps in the stools, which presented a much lower value than in the preceding periods.

To sum up, a food mixture composed of a high proportion of carbohydrate and low in fat resulted in a change in the general appearance of the stools, and in a fall of the mineral balance. There was noted also a marked change in the creatin output. The importance of the creatin values cannot be discussed at the present moment.

In the observations following the fourth period we aimed to change gradually the diet so as to raise principally the protein intake and to lower the fat and the carbohydrate. The highest protein intake was 6 per cent. of protein on the total volume of the food mixture.

During these periods the condition of the infant, as expressed by the daily gain in weight, was improved. The gain was 55 gm. per day the fifth, 64.8 gm. in the sixth, and 10.5 gm. per day in the seventh period.

14. Mendel, L. B., and Rose, W. C.: Jour. Biol. Chem., 1911, x, 213, 265.

15. Folin, Otto, and Dennis, W.: Jour. Biol. Chem., 1912, xi, 3, 253.

There was little change in the composition of the urine (Table 2) which could be considered of significance; perhaps worthy of note is again the creatin output, which still remained high; in fact, it reached its highest value during the fifth period. During that period the total calorific intake was lower than that of any of the preceding periods. In the following period the calorific intake was raised to 900 from 500, and with this change there was noted a fall in the creatin and simultaneously a rise in the creatinin output. During the following period in which the protein intake was raised to a still higher level, and the carbohydrate intake slightly increased, there was noted a still greater fall in the creatin and a still higher rise in the creatinin output. Thus it seems that in this infant the creatin output diminished with the increase of the protein intake. The proportion of carbohydrate in the food apparently had less influence on the output of creatin and creatinin.

However, the high protein intake caused a very striking change in the character of the stools (Table 3). They became for the most part pasty, grayish-yellow, smooth; in other words, practically normal. The total acidity showed a marked fall from 900 in the first period to 148 in the seventh period. On the contrary, the proportion of soaps was greatly increased, and with it followed an increased mineral retention.

The nitrogen retention during these periods reached its highest values. It is worthy of note, that the very high retention did not last more than one or two days after the beginning of the very high protein intake, and reached its equilibrium generally on the third day.

The most significant is the eighth period of observation (November 16 to November 21). The food at that period was so changed as to contain the same or a slightly higher proportion of protein, as in the previous period, with a lower intake of carbohydrate and fat, so as to bring down the average daily calorific intake to 632 calories. On this diet the infant seemed to remain in a normal condition for three days. On the fourth day, he developed high temperature, and other symptoms which are described in the clinical part of this communication. From the standpoint of chemical metabolism, this period presented nothing significant that could distinguish it from the preceding period. Everything that was said about the peculiarities of the urine, stools, and general balance of the preceding period applies also to this period.

The lower average values for the balances of nitrogen and other constituents are principally due to the fact that the child refused food during the days of high fever.

The only very striking peculiarity of this period was the retention of chlorids beginning a few days immediately preceding the fever and continuing during the days following it.

In the following ninth period (December 12 to December 23) a change of the diet was again made in the way of diminishing the protein to a minimum and raising the carbohydrate to a maximum. During this period the condition of the child and the character of the stools and urine were practically the same as during the third period of observation, when the carbohydrate intake was at its maximum.

The food of this period differed from that of the preceding periods not only in the proportion of fat, protein, and carbohydrate, but also in containing for part of the time sodium phosphate, which was added to the daily food mixture. However, this was without any effect on the body temperature.

The tenth period (December 26 to January 1) was planned to be a repetition of the observations made in the eighth period, and the food was made up in exactly the same way. This food is referred to as the "synthetic" food. Under the influence of that food the child remained in perfectly normal condition for five days, and on the sixth day he again developed a marked rise in body temperature which lasted until the following day.

Again there was observed a retention of chlorids beginning a few days preceding the fever and lasting after the body temperature was restored to normal.

CASE 2.—The observations were made on Jacob S., aged 7½ months. The observations on this infant and also on Case 3 are divided into periods corresponding to food changes. These changes were planned to furnish definite evidence as to whether or not the "synthetic" food mixture was capable of disturbing the normal body temperature. With this in view the food intake was gradually modified so as to preserve approximately the same calorific intake by replacing the carbohydrate with protein until the maximum protein intake of 6 per cent. of the food mixture was reached.

The general changes in the composition of the urine and stools had the same character as in the periods of high protein intake of the first infant, namely, there was noted a gradual fall in the acidity of the stools and with it a rise in the proportion of soaps and general increase in the mineral balance. The nitrogen retention steadily increased until the maximum protein intake was reached. The child was gaining in weight continually, though slowly, and the total gain was about 350 gm.

When the highest protein intake of 6 per cent. per day was reached, the food was again changed to the one designated as "synthetic" mixture. On the fourth day of that régime the infant developed fever reaching 103.2 F. This fever continued for seven days until the food was changed. The general character of the stools, urine, and general metabolism presented nothing of significance that distinguished the period of "synthetic" diet from the immediately preceding period. Typical only was the retention of chlorids as noted in both observations on Case 1. The changes that are recorded in the last days of this period were not due to the character of the food, but to the administration of calomel and castor-oil, which caused free catharsis.

Two series of observations were made on Case 3, Francis D. The first one aimed simply to determine the capacity of the "synthetic" food mixture to cause a rise in body temperature (Table 5). There was no investigation made into the chemical metabolic changes. The results of this observation were in all respects confirmatory of the first three observations made on the other infants. Fever developed on the fourth day.

The second series of observations made on this infant was planned principally to ascertain whether the influence of the "synthetic" food mixture on the body temperature is a constant occurrence; during this period clinical observations were accompanied by a study of the chemical metabolism. Again on this occasion the changes of the diet aimed principally at raising the protein intake to a maximum of 6 per cent. of the milk formula. The food mixture contained 5 per cent. of protein when the infant was first placed in the metabolism bed. In the course of four days the maximum of 6 per cent. was reached, and this was continued for sixteen days. There was a constant gain in weight and a constant rise in the nitrogen retention. The general changes in the composition of the urine and feces were the same as in the other experiments. The most striking features were the fall in the total acidity of the feces, the rise in the proportion of soap, and the rise in the mineral balance.

After the child had been for sixteen days on the maximum protein intake, the diet was again changed to the "synthetic" food mixture. On the fourth day after this change there was again a marked rise of the body temperature which reached on the fifth day of the period 104 F. The addition of lactose, raising the carbohydrate to 5 per cent., had no effect on the temperature, though it was continued for two days. The condition of the infant, however, did not permit of prolonging the observation and on the seventh day of this period the "synthetic" food was discontinued. The general character of the urine and stools during this period did not present any striking differences from that of the previous ones, and those differences that did appear may be explained by looseness of the bowels produced by prolonged administration of milk of magnesia. There was again noted the usual retention of chlorids.

TABLE 2.—AVERAGE DAILY FOOD INTAKE

CASE 1, FRANCIS H.

Period	Dates	Composition of Food	Volume In- take c.c.	Fat, gm.	Carbohydrate, gm.	Protein, gm.	Nitrogen, gm.	Total Number Calories	Chloride as NaCl, gm.	Phosphates as P ₂ O ₅ , gm.	Total Ash as Oxide, gm.	CaO, gm.
1	Sept. 14 to Oct. 3	Sixty-five per cent. milk, 5 per cent. lime water, barley water to volume, making fat 2.6 per cent., protein 2.4 per cent.; lactose added to make 5 per cent.	1,255	32.4	57.0	29.8	4.76	721	1.68	2.58	7.46	2.55
2	Oct. 4-14	Like that of Period 1, except that no lactose added, making carbohydrate 3 per cent.	1,260	33.6	48.5	27.4	4.54	690	1.68*	2.55	7.60	3.21
3	Oct. 16-19	Fat-free milk, cane-sugar added to make total carbohydrate 6 per cent.; protein 3.5 per cent.	1,260	0	75.5	41.3	6.61	567	1.57	2.77	9.86	3.65
4	Oct. 20-24	Mixture of fat-free and full milk, making 1.6 per cent. fat and 3.0 per cent. protein; cane-sugar to make 4.7 per cent. carbohydrate; 10 per cent. barley-water, 5 per cent. lime-water included.	1,260	20.0	59.6	34.8	5.57	649	1.88	2.40	8.88	3.01
5	Oct. 25-29	Three-fourths ordinary protein milk, $\frac{1}{4}$ barley-water, making fat 1.9 per cent., carbohydrate 2.3 per cent., protein 2.9 per cent.	1,230	23.0	28.0	35.7	5.71	504	1.26	2.21	7.71	2.80
6	Oct. 31 to Nov. 6	Protein milk made from casein of 2 liters full milk, 1 liter ripened fat-free milk and 120 c.c. water, making fat 3.6 per cent., carbohydrate 3.1 per cent., protein 5.6 per cent.	1,243	44.2	38.7	69.5	11.12	913	2.23	4.0	13.13	2.52
7	Nov. 14-16	Protein milk made from casein of 1 liter full milk, 1 liter ripened fat-free milk and 120 c.c. water, 4 drams maltose to day's food, making fat 3.5 per cent., carbohydrate 3.4 per cent., protein 3.9 per cent.	1,260	43.5	42.7	49.6	7.94	845	1.81	3.14*	10.28	2.72
8	Nov. 16-21	So-called synthetic food, fat 2.9 per cent., carbohydrate 1.5 per cent., protein 5.8 per cent. For description see text.	1,260	31.8	18.5	71.6	11.46	705	.730†	3.60†	11.70	3.37†
			1,260	36.6	18.9	65.4	10.44	722	10.58
			1,260	39.7	20.3	78.0	12.48	815	11.82
			1,135	33.8	17.3	68.4	10.94	702	9.85
			580	15.7	8.6	36.8	5.9	365	5.47
9	Dec 12-16 16-20 20-23	Mixture fat-free and full milk, making fat 2 per cent., protein 2.5 per cent.; dextrimaltose added to make carbohydrate 6.4 per cent.; 20 per cent. barley-water and 5 per cent. lime-water included. In part of period (Dec. 16-20) 8.3 gm. mono- and disodium phosphate added to day's food.	1,260	26.2	72.4	31.0	4.96	732	1.59†	2.47†	6.99	1.56†
			1,260	20.6	85.0	31.3	5.0	728	14.94
			1,260	29.9	85.9	31.0	4.96	818	8.91
10	Dec. 26 to Jan. 1	So-called synthetic food, fat 2.1 per cent., carbohydrate 1.7 per cent., protein 6.3 per cent.	515	10.6	8.0	31.2	4.99	480†	.587†	2.90†	4.78	3.18†
			1,045	27.9	18.7	63.7	10.19	7.45
			1,135	26.1	19.6	72.7	11.63	10.49
			1,184	23.8	19.9	59.5	12.30	9.94

Daily Figures

Daily Figures

1	Feb. 27-29	Mixture fat-free and full milk to make fat 1.45 per cent., protein 3.5 per cent., lactose added to make 5 per cent.; 2 dr. neutral maltose and 3½ dr. olive oil added to day's food.....	1,050	26.6	52.2	33.7	5.39	676	1.13	2.25	5.41	1.98
2	Feb. 29 to March 4	Fat 1.45 per cent., carbohydrate 4.5 per cent., protein 4 per cent., 3½ dr. olive oil added to day's food. For method of making up this formula and the four following see text.....	998	27.1	45.6	40.7	6.50	637	1.01	2.53	5.26	2.12
3	March 4-7	Fat 1.45 per cent., carbohydrate 4.0 per cent., protein 4.5 per cent., 3½ dr. olive oil added to day's food	1,007	29.1	40.5	42.6	6.82	647	1.19	2.48	5.47	2.28
4	March 7-10	Fat 1.45 per cent., carbohydrate 3.5 per cent., protein 5.0 per cent., 3½ dr. olive oil added to day's food	1,015	24.9	37.8	51.9	8.31	636	1.40	2.99	6.45	2.37
5	March 10-13	Fat 1.45 per cent., carbohydrate 3.0 per cent., protein 5.5 per cent., lime-water 5 per cent., 3½ dr. olive oil in day's food	1,025	24.3	32.8	57.0	9.12	628	1.23	3.22	6.66	2.74
6	March 13-18	Fat 1.45 per cent., carbohydrate 2.1 per cent., protein 6.0 per cent., lime-water 5 per cent., 1½ dr. olive oil in day's food	1,050	16.7	28.6	61.6	9.85	563	1.19	3.64	7.97	3.35
7	March 18-27	So-called synthetic food, fat 1.45 per cent., carbohydrate 1.8 per cent., protein 6.0 per cent., 1½ dr. olive oil added to day's food; 120 c.c. breast milk March 25 and 210 c.c. March 26.	900	14.7	13.8	47.9	7.67	397	.327	2.49	6.13	2.77
			1,050	15.2	19.8	66.0	10.56	502	.574	3.44	7.66	2.77
			975	17.1	19.0	59.9	9.60	491	.615	2.98	7.54	3.44
			630	14.2	11.8	35.8	5.74	333	.242	1.98	4.34	2.98
			900	16.2	19.2	60.4	9.68	486	.463	3.22	6.66	2.98
			780	14.3	15.3	53.2	8.51	421	.434	2.82	6.27	2.96
			1,050	14.1	19.8	65.6	10.50	490	.642	3.49	7.75	3.76
			930	14.9	23.9	50.4	8.07	448	.400	2.74	6.29	2.62
			725	14.8	24.9	35.2	5.64	386	.300	1.90	4.08	1.99

Daily Figures

CASE 3, FRANCIS D.

1	May 1	Fat 2.6 per cent., carbohydrate 4.5 per cent., protein 5.0 per cent., 2 dr. olive oil added to day's food	1,260	38.2	65.8	63.4	10.13	917	1.44	3.84	7.65	3.24
2	May 2-4	Fat 2.6 per cent., carbohydrate 3.5 per cent., protein 5.5 per cent., 2 dr. olive oil in day's food	1,260	38.0	46.0	71.4	11.42	877	1.49	4.12	9.34	3.71
3	May 4-19	Fat 2.6 per cent., carbohydrate 2.5 per cent., protein 6.0 per cent., 2 dr. olive oil in day's food. For method of making up this and two preceding formulæ see text	1,253	38.6	33.8	74.9	11.98	846	1.47	4.23	10.50	4.12
4	May 20-24	So-called synthetic food, fat 2.6 per cent., carbohydrate 1.8 per cent., protein 6.0 per cent., 2 dr. olive oil in day's food; 36 gm. lactose added to day's food May 23-24.	1,260	36.2	22.0	73.4	11.75	739	.253	3.75	8.65	3.36
			1,260	41.4	22.0	74.8	11.95	794	.360	3.95	9.95	4.17
			1,260	40.2	21.9	71.2	11.40	767	.256	3.62	9.11	3.69
			1,260	37.5	21.8	76.5	12.24	764	.369	1.13	9.60	3.85
			1,260	36.4	58.2	69.0	11.06	863	.167	3.61	7.99	3.39

Daily Figures

* Estimated. † Average.

TABLE 3.—URINE CONSTITUENTS. AVERAGE DAILY VALUES

CASE 1, FRANCIS H.

Period	Dates	Volume, c.c.	Specific Gravity	Indican	Total Nitrogen, gm.	Ammonia Nitrogen, gm.	Ammonia Nit. Per cent. Total N.	Kreatinin, gm.	Kreatin Nitrogen, gm.	Inorg. Sulphates as H ₂ SO ₄ , gm.	Ethereal Sulphates as H ₂ SO ₄ , gm.	Total Sulphates as H ₂ SO ₄ , gm.	Chlorides as NaCl, gm.	Phosphates as P ₂ O ₅ , gm.	Total Ash as Oxids, gm.	CaO, gm.
1	Sept. 14 to Oct. 3	426	1.010½	Gen. Negative	2.31	.240	8.5	.063	.023	.362	.123	.485	.817	.587	1.44	.079
2	Oct. 4-14	541	1.011	Neg. to High 10+	3.18	.118	3.7	.055	.011	.472	.131	.603	1.179	.635	2.72
3	Oct. 16-19	547	1.013	Negative	4.66	.152	3.2	.043	.047	.722	.122	.844	1.549	.731	3.39
4	Oct. 20-24	663	1.011	Negative	4.29	.073	1.7	.050	.078	.772	.080	.852	1.894	.729	4.45	.673
5	Oct. 25-29	703	1.011	Faint trace or neg.	4.78	.132	2.8	.042	.108	.695	.139	.834	1.791	.577	2.48
6	Oct. 31 to Nov. 6	488	1.018	Neg. or small trace	7.45	.342	4.6	.064	.055	1.078	.133	1.211	1.392	.832	3.21	.124
7	Nov. 14-16	475	1.016	Nearly negative	5.36	.158	3.0	.075	.008	.747	.188	.935	.806	.612	2.84
8	Nov. 16-21	550	1.012	Faint trace	5.30	.137	2.6	.071	.025	.671	.219	.890	.323	.636	1.69
		490	1.016	Faint trace	7.52	.178	2.4	.070	.059	1.129	.040	1.169	0	.639	1.65
		530	1.016	Trace	8.76	.279	3.2	.074	.008	1.122	.172	1.294	0	.780	1.59
		475	1.018	8-10	9.34	.328	3.4	.070	.008	.798	.568	1.356	0	.722	1.33
		350	1.019	16-20	7.36	.340	4.6	.081	.004	1.22	.165	1.385	0	.717	1.44
9	Dec. 12-16	514*	1.013*	Negative	3.35	.189	5.7	.043	.029	.523	.087	.610	1.53	.516	3.45	2.30*
	16-20	3.08	.187	5.7	.041	.008	.492	.065	.547	1.55	.757	4.31
	20-23	3.30	.158	4.8	.041	.042	.538	.080	.618	1.98	.566	4.07
10	Dec. 26 to Jan. 1	255	1.021*	Negative	3.70	.110	3.0	.044	.010	.632	.045	.677	.513	.582	2.01	.028*
		330	Large trace	6.65	.337	5.1	.055	.023	.904	.062	.966	.292	.747	1.77
		430	Trace	7.98	.344	4.3	.043	.020	.982	.019	1.001	.066	.525	1.52
		410	Faint trace	9.10	.327	3.6	.044	.0	1.185	.017	1.202	0	.665	1.31
		390	8-10	8.80	.405	4.6	.054	.027	1.124	.011	1.135	0	.642	1.72
		355	Trace	7.10	†047	1.185	.094	1.279	0	.686	1.77

TABLE 4.—COMPOSITION OF FECES. AVERAGE DAILY VALUES

CASE 1, FRANCIS H.

Period	Dates	Dried Weight, gm.	Dried Weight, per cent. of Moist.	Water in Feces, c.c.	Total Nitrogen, gm.	Total Nitrogen, %	Chlorid as NaCl, gm.	Phosphates as P ₂ O ₅ , gm.	Total Ash as Oxids, gm.	Total Ash % of Dried Weight	CaO, gm.	Total Fat, gm.	Total Fat, per cent. Dried Weight	Neutral Fat, gm.	Neutral Fat per cent. Total Fat	Free Ratty Acids, gm.	Ratty Acids per cent. Total Fat	Soap Fat, gm.	Soap Fat, per cent. Total Fat	Total Acidity for 24 Hours c.c. N/10 NaOH	Total Acidity per 100 gm. Dried Wt.	Volatile Acids, 24 Hours, c.c. N/10 NaOH	Volatile Acids per 100 gm. Dried Wt.
1	Sept. 14 to Oct. 3	19.9	7.8	251	.782	4.0	.60	.92	3.98	20.0	1.28	6.96	34.7	4.72	66.2	1.18	16.8	1.06	17.0	181.6	903	118.6	639
2	Oct. 4-14	15.4	8.0	191	.707	4.6	.49	.80	4.56	29.6	1.34	4.61	29.5	2.94	63.6	.80	16.1	.87	20.3	119.9	779	137.3	907
3	Oct. 16-19	16.8	8.4	195	.922	5.5	.19	1.53	5.93	35.4	2.33	.43	3.9	.43	100.	133.3	799	110.0	658
4	Oct. 20-24	12.4	8.9	128	.587	4.7	.23	1.08	4.07	32.8	1.44	1.77	14.2	1.30	72.0	.25	16.2	.22	11.8	93.1	752	112.8	872
5	Oct. 25-29	7.7	16.2	40	.340	4.4	.05	0	2.87	37.0	1.27	1.23	15.6	.60	50.7	.12	7.9	.51	41.4	13.3	169	68.9	902
6	Oct. 31 to Nov. 6	16.6	16.5	88	.663	4.0	.09	1.89	6.06	36.4	2.73	3.75	22.8	1.08	29.6	.14	4.3	2.53	66.1	25.6	148	128.0	757
7	Nov. 14-16	13.5	18.0	73	.594	4.4	.02	1.47	4.90	36.2	1.96	2.15	17.3	.65	27.6	.13	6.7	1.37	65.7	40.3	148	125.5	927
8	Nov. 16-21	15.0	13.7	95	.547	3.6	.17	1.87*	6.05	40.3	2.62*	2.72	18.1	1.38	50.8	.03	2	1.31	48.1	52.6	351	122.0	812
9	Daily Figures	11.7	21.0	44	.336	2.9	.02	4.66	39.8	...	4.53	38.6	.88	19.4	.15	3.1	3.50	77.5	76.3	65	93.5	797
		15.4	24.4	48	.443	2.9	.02	5.05	32.8	...	6.82	44.2	1.81	26.5	.63	9.3	4.38	64.2	19.0	123	148.5	964
		9.6	32.7	20	.296	3.1	0	3.18	33.2	...	4.16	43.4	.87	20.9	.40	9.7	2.89	69.4	8.9	93	53.9	562
		35.6	22.9	120	.856	2.4	0	10.85	30.6	...	19.20	54.0	6.16	32.0	.96	5.0	12.08	63.0	78.0	219	240.8	628
10	Daily Figures	12.9	11.7	99	.609	4.7	.11*	1.34*	3.49	26.9	1.91*	2.29	17.8	1.60	70.2	.35	15.4	.34	14.4	71.8	551	130.9	1,012
		12.5	8.2	142	.511	4.1	4.58	36.5	...	2.06	16.4	1.55	73.5	.48	24.9	.03	1.6	84.2	666	114.6	931
		11.8	11.1	96	.502	4.3	3.62	30.9	...	2.15	18.1	1.05	49.0	.43	18.4	.66	32.6	59.4	505	117.4	1,015
		3.1	14.6	18	.207	6.8	.08*	1.88*	.80	26.3	3.55*	.88	29.0	.42	48.0	.22	24.8	.24	27.2	6.7	218	106.2	3,490
10	Daily Figures	16.5	20.8	63	.807	4.9	5.38	32.7	...	2.75	16.7	1.20	43.7	.26	9.6	1.29	40.7	23.1	140	137.8	838
		20.0	15.3	111	.960	4.8	7.07	35.4	...	3.46	17.3	2.46	71.1	0	0	1.00	28.9	21.2	106	188.0	943
		12.0	15.4	66	.616	5.1	3.68	30.8	...	5.72	18.6	.90	40.3	0	0	1.32	53.7	32.5	272	118.0	989
		25.5	18.1	116	1.188	4.7	8.83	34.6	...	8.02	22.4	2.52	44.2	.59	10.3	2.61	45.5	61.1	239	183.0	718
10	Daily Figures	22.9	20.3	90	.897	3.9	5.72	25.0	...	8.02	35.0	5.99	74.9	2.03	25.1	0	0	100.8	440	166.5	728

CASE 2, JACOB S.

	1	2	3	4	5	6	7	Daily Figures																					
	Feb. 27-29	Feb. 29 to March 4	March 4-7	March 7-10	March 10-13	March 13-18	March 18-27	11.6	15.9	62	.672	5.8	.04	1.25	3.35	28.9	1.58	1.63	13.1	.70	45.4	.58	37.8	.26	16.8	51.4	442	99.0	853
								8.7	21.2	32	.506	5.8	.02	1.13	2.54	29.4	1.42	1.45	16.7	.73	50.3	.02	1.4	.70	48.3	22.0	254	92.6	1,068
								15.4	14.8	89	.855	5.6	.06	1.66	4.12	26.8	2.22	3.56	23.2	1.79	50.2	.97	27.1	.81	22.7	77.4	504	135.6	883
								10.8	15.5	59	.685	6.4	.12	1.55	3.22	29.8	1.75	.74	6.8	.45	60.8	0	0	.29	30.2	33.1	307	109.0	1,011
								9.8	26.9	27	.546	5.6	.05	1.61	3.41	34.7	1.92	.73	7.4	.30	41.1	.07	9.6	.36	49.3	3.4	35	93.3	951
								11.5	31.4	25	.576	5.0	.04	1.81	4.18	36.4	2.52	1.28	11.1	.42	32.8	0	0	.86	67.2	3.6	31	112.2	975
								9.2	29.1	23	.450	4.9	.03	1.58	3.67	39.7	1.98	.83	9.0	.14	16.7	0	0	.69	83.3	5.5	60	73.9	801
								5.2	33.8	10	.264	5.0	.01	.62	2.12	40.5	1.15	.15	2.9	.12	75.9	0	0	.04	24.1	4.8	91	119.0	2,275
								8.6	32.4	18	.430	5.0	.03	1.46	3.55	41.3	1.88	1.16	13.5	.27	23.0	.06	5.2	.83	71.8	0	0	104.0	1,213
								46.7	21.6	170	2.519	5.4	.17	4.66	11.25	24.1	3.22	10.84	23.2	7.66	70.7	.14	1.3	3.04	28.0	168.3	360	336.0	719
								28.1	16.9	138	2.454	8.7	.17	1.92	3.86	13.7	2.06	6.04	17.9	4.98	98.9	.06	1.1	0	0	183.6	662	164.0	848
								26.8	18.0	166	2.411	9.0	.25	2.00	4.55	17.0	2.60	5.16	12.3	4.76	92.2	0	0	.40	7.8	245.0	916	177.2	908
								21.4	12.5	187	1.575	7.8	.27	1.62	3.56	16.7	1.90	6.16	12.3	3.06	91.7	.08	0	0	0	120.0	992	182.4	923
								28.2	12.5	187	1.575	7.8	.27	1.62	3.56	16.7	1.90	6.16	12.3	3.06	91.7	.08	0	0	0	120.0	992	182.4	923

CASE 3, FRANCIS D.

	May 1	20.2	18.4	90	.785	3.9	.10	.88	3.54	17.5	2.34	9.53	47.1	1.46	15.2	.44	4.7	7.63	80.1	40.5	200	162.4	803
1	May 1	16.4	17.5	72	.859	3.9	.10	.86	3.34	21.6	1.87	6.31	40.9	1.54	24.4	.05	.77	4.72	74.9	26.6	173	203.0	1,318
2	May 2-4	17.8	13.5	114	.694	3.9	.20	1.49	4.87	27.3	2.73	5.27	29.6	1.01	19.2	.07	1.3	4.19	79.5	29.6	166	131.8	740
3	May 4-19	13.8	12.3	98	.626	4.6	.27	1.30	3.81	27.7	2.18	4.47	32.5	1.22	27.4	0	0	3.25	72.6	23.8	173	124.5	907
4	May 20-24	12.1	13.2	79	.605	5.0	.18	.86	2.42	20.1	1.26	4.20	34.8	1.79	42.6	.59	14.1	1.82	43.3	50.3	417	125.0	1,038
	Mean	27.3	11.0	220	1.470	5.4	.62	1.98	6.06	22.2	3.25	9.30	33.6	4.34	46.7	3.99	42.9	.97	10.4	139.0	509	320.0	1,173
	Dev.	17.9	9.3	174	1.013	5.7	.75	1.11	3.57	20.0	1.78	6.42	30.3	2.70	49.8	.99	18.2	1.73	32.0	111.1	623	182.8	1,023
	St. Dev.	25.9	11.4	201	1.422	5.5	.46	1.54	4.48	17.3	2.14	6.91	26.7	4.50	65.2	0	0	2.41	34.8	163.0	631	204.0	789

DESCRIPTION OF FECES

CASE 1, FRANCIS H.

1. Sept. 14-Oct. 3.—Thin, generally very watery, containing fat curds and few small hard curds, greenish-yellow, sometimes foamy; 8-12 stools daily.
2. Oct. 4-14.—Becoming more solid than in Period 1, more finely granular, 7-9 stools daily.
3. Oct. 16-19.—Orange-yellow, pasty or watery, containing hard curds and considerable mucus; 11-13 stools daily.
4. Oct. 20-24.—Watery or pasty, smooth and finely granular, containing small fat and protein curds, less mucus than in Period 3; 8-10 stools daily.
5. Oct. 25-29.—Mostly formed but soft, yellow-gray, smooth; 3-4 stools daily.
6. Oct. 31-Nov. 6.—Mostly formed, smooth, harder than in Period 5, portions watery or pasty, granular; 4-6 stools daily.
7. Nov. 14-16.—About as in Period 6; 4-5 stools daily.
8. Nov. 16-21.—After first day formed, hard and dry, containing fragments of hard curds; 3-6 stools daily.
9. Dec. 12-23.—Pasty or watery, containing fat curds, hard curds, and mucus, acid and rancid; 4-10 stools daily; more solid during last three days with less mucus.
10. Dec. 26-Jan. 1.—At first formed and semi-formed, rather soft and mealy, becoming hard and dry. After castor-oil was given largely watery and pasty, with small hard curds; 4-7 stools daily.

CASE 2, JACOB S.

1. Feb. 27-29.—Pasty, slightly formed, partly fluid, granular with fat curds, partly greenish; 4 stools daily.
2. Feb. 29-March 4.—Mostly formed, yellow-gray, smooth; 1-5 stools daily.
3. March 4-7.—More watery than in Period 2, foul, partly greenish, small part formed, 2-5 stools daily.
4. March 7-10.—As in preceding period, but generally more formed; 2-3 stools daily.
5. March 10-13.—Formed and hard; foul; 3-6 stools daily.
6. March 13-18.—As in preceding period, often with traces of blood; 3-7 stools daily.
7. March 18-27.—As in preceding period; 2-4 stools daily, until after castor-oil was given, then thin, pasty and watery, containing fragments of hard curds and mucus, generally greenish; 7-8 stools daily.

CASE 3, FRANCIS D.

1. May 1.—Formed, smooth, portion dry and hard, larger part soft, yellow-gray, 4 stools.
2. May 2-4.—As in Period 1; 1-4 stools daily.
3. May 4-19.—For first six days as in Periods 1 and 2, after that larger part thinner and less formed, 1-4 stools daily.
4. May 20-24.—Mostly watery and pasty, containing hard curds and often mucus, in increasing amount, partly greenish; about 3 stools daily.

TABLE 5.—BALANCES. AVERAGE DAILY VALUES

CASE 1, FRANCIS H.

Period	Dates	Total Nitrogen Retained, gm.	Nitrogen Retained, per cent. Intake	Nitrogen Retained, per cent. Absorbed	Nitrogen Absorbed, per cent. Intake	Total Fat Absorbed, gm.	Fat Absorbed, per cent. of Intake	Chlorid as NaCl Retained, gm.	Phosphates as P ₂ O ₅ Retained, gm.	Total Ash as Oxids Retained, gm.	CaO Retained, gm.	Gain or Loss in Body Weight, gm.	Weight Beg. and End of Period, gm.
1	Sept. 14 to Oct. 3	+1.17	24.5	29.4	83.5	+25.5	78.6	+258	+1.07	+2.04	+1.19	+ 11.7	4,330
2	Oct. 4-14	+ .65	14.4	17.1	84.7	+29.0	86.5	+0.14	+1.12	+ .32	+1.87	+ 4.6	4,553
3	Oct. 16-19	+1.03	15.6	18.1	86.2	0	—17	+ .51	+ .54	+1.32	+25.7	4,683
4	Oct. 20-24	+ .69	12.4	13.9	89.6	+18.2	91.0	—25	+ .59	+ .36	+ .90	— 23.3	4,858
5	Oct. 25-29	+ .60	10.4	11.1	94.1	+21.8	94.8	—58	+1.63	+2.36	+1.53	+55.3	4,884
6	Oct 31 to Nov. 6	+3.01	27.0	28.7	94.2	+40.5	91.6	+75	+1.28	+3.86	— .33	+ 64.8	4,791
7	Nov. 14-16	+1.99	25.1	27.1	92.7	+41.3	95.0	+98	+1.06	+2.54	+ .76	+ 10.5	4,593
8	Nov. 16-21	+5.62 +2.58 +3.28 +1.30 —2.32	49.1 24.7 26.3 11.9	51.4 25.5 27.3 12.3	95.3 96.7 96.5 97.3 84.9	+29.1 +32.1 +32.9 +29.6 — 3.5	91.5 87.9 82.8 87.7	+588*	+1.027*	+3.97 +4.27 +4.98 +5.35 —6.82	+ .75*	+47.0 + 1.0 +72.0 —70.0 —497.0	5,016 5,063 5,064 5,136 5,066
9	Dec. 12-16	+1.00	20.2	23.1	87.9	+23.9	91.4	—05	+ .61	+ .06	— .35*	— 30.3	4,569
	16-20	+1.41	28.2	31.4	89.9	+18.6	90.4	—07	+ .37	+6.05	+ 50.3	5,206
	20-23	+1.16	23.3	26.0	90.1	+27.8	93.1	—50	+ .56	+1.22	+ 9.0	5,085
10	Dec. 26 to Jan. 1	+1.08 +2.73 +2.69 +3.48 +2.51 —6.06	21.8 26.8 23.1 26.4 20.1	22.7 29.2 25.2 27.7 22.2	96.1 92.1 91.8 95.3 90.6 53.8	+ 9.72 +25.2 +22.6 +21.6 — 4.3	91.6 90.2 90.3 90.6 75.7	+358*	+ .384*	+1.37 + .30 +1.90 +4.95 +1.23 —5.88	— .40*	—276.0 +226.0 + 27.0 —33.0 +109.0 —697.0	5,265 4,989 5,215 5,242 5,209 5,318 4,621

CASE 2, JACOB S.

1	Feb. 27-29	+1.89	35.1	40.0	87.7	+25.1	94.2	+22	+ .42	-1.18	+ .38	+ 92.0	3,968
2	Feb. 29 to March 4	+1.62	25.0	27.0	92.4	+25.6	94.8	+08	+ .83	+ .75	+ .66	+ 14.0	4,161
3	March 4-7	+1.17	17.1	19.5	87.6	+25.5	87.9	+131	+ .268	- .26	+ .04	- 6.0	4,151
4	March 7-10	+1.77	21.3	23.2	91.8	+24.2	97.2	+437	+ .78	+1.20	+ .61	+ 29.0	4,208
5	March 10-13	+2.13	23.6	25.1	94.0	+23.6	97.1	+128	+1.01	+1.63	+ .89	+ 16.0	4,191
6	March 13-18	+1.62	16.4	17.4	94.2	+15.4	92.3	+029	+1.08	+1.74	+ .78	+ 19.0	4,278
7	March 18-27	+1.22	15.9	16.9	94.2	+13.8	94.5	-42	+ .31	+ .86	+ .80	- 75.0	4,326
		+3.98	37.7	38.7	97.8	+15.1	99.0	+28	+2.17	- 60.0	4,423
		+1.34	14.0	14.6	95.6	+15.9	93.4	+14	+ .77	+2.34	+1.56	- 19.0	4,348
		-3.20	56.1	+ 3.4	23.6	-39	-3.29	-8.17	-4.14	-313.0	4,408
		+1.98	20.5	27.4	74.9	+11.1	68.6	+11	+ .65	+1.78	+ .88	- 21.0	4,389
		- .15	71.7	+ 9.11	63.8	+10	+ .20	+ .67	+ .04	- 35.0	4,076
		+3.66	34.8	41.4	84.0	+10.8	76.4	+29	+1.46	+3.28	+1.86	+ 21.0	4,055
		+ .15	1.9	2.6	72.4	+ 8.9	60.0	-20	+ .20	+ .43	+ .30	- 46.0	4,020
		- .90	70.2	+11.4	77.4	-08	+ .09	+ .49	+ .34	-127.0	4,041
													3,895
													3,868

CASE 3, FRANCIS D.

1	May 1	+2.96	29.2	31.7	92.2	+28.6	75.2	+768	+1.63	+1.58	+ .80	+147.0	4,725
2	May 2-4	+3.32	29.0	30.5	95.2	+31.7	83.5	+505	+1.74	+3.16	+1.74	- 41.0	4,872
3	May 4-19	+3.42	28.5	30.3	94.3	+33.3	86.4	+502	+1.42	+3.10	+1.29	+ 18.0	4,872
4	May 20-24	+3.47	29.5	31.2	94.7	+31.7	87.7	-192	+1.32	+2.68	+1.18	+ 71.0	4,790
		+6.56	54.9	57.8	94.9	+37.2	89.8	+161	+2.34	+6.07	+2.90	- 61.0	5,077
		+2.40	21.1	24.2	87.1	+30.9	76.9	-360	+ .62	+1.04	+ .44	- 83.0	5,148
		+2.77	22.6	24.6	91.8	+32.1	85.7	-390	+1.66	+3.51	+2.07	- 8.0	5,087
		+2.27	20.5	23.6	87.1	+29.5	81.1	-295	+ .98	+1.38	+1.25	-203.0	5,004
													4,996
													4,793

TABLE 2.—AVERAGE DAILY FOOD INTAKE

CASE 1, FRANCIS H.

Period	Dates	Composition of Food	Volume In- take c.c.	Fat, gm.	Carbohydrate, gm.	Protein, gm.	Nitrogen, gm.	Total Number Calories	Chloride as NaCl, gm.	Phosphates as P ₂ O ₅ , gm.	Total Ash as Oxide, gm.	CaO, gm.
1	Sept. 14 to Oct. 3	Sixty-five per cent. milk, 5 per cent. lime water, barley water to volume, making fat 2.6 per cent., protein 2.4 per cent.; lactose added to make 5 per cent.	1,255	32.4	57.0	29.8	4.76	721	1.68	2.58	7.46	2.55
2	Oct. 4-14	Like that of Period 1, except that no lactose added, making carbohydrate 3 per cent.	1,260	33.6	48.5	27.4	4.54	690	1.68*	2.55	7.60	3.21
3	Oct. 16-19	Fat-free milk, cane-sugar added to make total carbohydrate 6 per cent.; protein 3.5 per cent.	1,260	0	75.5	41.3	6.61	567	1.57	2.77	9.86	3.65
4	Oct. 20-24	Mixture of fat-free and full milk, making 1.6 per cent. fat and 3.0 per cent. protein; cane-sugar to make 4.7 per cent. carbohydrate; 10 per cent. barley-water, 5 per cent. lime-water included.	1,260	20.0	59.6	34.8	5.57	649	1.88	2.40	8.88	3.01
5	Oct. 25-29	Three-fourths ordinary protein milk, ¼ barley- water, making fat 1.9 per cent., carbohydrate 2.3 per cent., protein 2.9 per cent.	1,230	23.0	28.0	35.7	5.71	504	1.26	2.21	7.71	2.80
6	Oct. 31 to Nov. 6	Protein milk made from casein of 2 liters full milk, 1 liter ripened fat-free milk and 120 c.c. water, making fat 3.6 per cent., carbohydrate 3.1 per cent., protein 5.6 per cent.	1,243	44.2	38.7	69.5	11.12	913	2.23	4.0	13.13	2.52
7	Nov. 14-16	Protein milk made from casein of 1 liter full milk, 1 liter ripened fat-free milk and 120 c.c. water, 4 drams maltose to day's food, making fat 3.5 per cent., carbohydrate 3.4 per cent., protein 3.9 per cent.	1,260	43.5	42.7	49.6	7.94	845	1.81	3.14*	10.28	2.72
8	Nov. 10-21	So-called synthetic food, fat 2.9 per cent., car- bohydrate 1.5 per cent., protein 5.8 per cent. For description see text.	1,260	31.8	18.5	71.6	11.46	705	.730†	3.60†	11.70	3.37†
			1,260	36.6	18.9	65.4	10.44	722	10.58
			1,260	39.7	20.3	78.0	12.48	815	11.62
			1,135	33.8	17.3	68.4	10.94	702	9.85
			580	15.7	8.6	36.8	5.9	355	5.47
9	Dec 12-16 16-20 20-23	Mixture fat-free and full milk, making fat 2 per cent., protein 2.5 per cent.; dextrimaltose added to make carbohydrate 6.4 per cent.; 20 per cent. barley-water and 5 per cent. lime- water included. In part of period (Dec. 16- 20) 8.3 gm. mono- and disodium phosphate added to day's food.	1,260	26.2	72.4	31.0	4.96	732	1.59†	2.47†	6.99	1.50†
			1,260	20.6	85.0	31.3	5.0	728	14.94
			1,260	29.9	86.9	31.0	4.96	818	8.91
10	Dec. 26 to Jan. 1	So-called synthetic food, fat 2.1 per cent., carbo- hydrate 1.7 per cent., protein 6.3 per cent.	515	10.6	8.6	31.2	4.99	480†	.587†	2.90†	4.78	3.16†
			1,045	27.9	18.7	63.7	10.19	7.45
			1,135	26.1	19.6	72.7	11.63	10.49
			1,184	23.8	19.6	82.5	13.20	9.94
			1,280	23.5	20.4	79.2	12.50	11.78

Daily Figures

Daily Figures

1	Feb. 27-29	Mixture fat-free and full milk to make fat 1.45 per cent., protein 3.5 per cent., lactose added to make 5 per cent.; 2 dr. neutral maltose and 3½ dr. olive oil added to day's food.....	1,050	26.6	52.2	33.7	5.39	676	1.13	2.25	5.41	1.98
2	Feb. 29 to March 4	Fat 1.45 per cent., carbohydrate 4.5 per cent., protein 4 per cent., 3½ dr. olive oil added to day's food. For method of making up this formula and the four following see text.....	998	27.1	45.6	40.7	6.50	637	1.01	2.53	5.26	2.12
3	March 4-7	Fat 1.45 per cent., carbohydrate 4.0 per cent., protein 4.5 per cent., 3½ dr. olive oil added to day's food	1,007	29.1	40.5	42.6	6.82	647	1.19	2.48	5.47	2.28
4	March 7-10	Fat 1.45 per cent., carbohydrate 3.5 per cent., protein 5.0 per cent., 3½ dr. olive oil added to day's food	1,015	24.9	37.8	51.9	8.31	636	1.40	2.99	6.45	2.37
5	March 10-13	Fat 1.45 per cent., carbohydrate 3.0 per cent., protein 5.5 per cent., lime-water 5 per cent., 3½ dr. olive oil in day's food.....	1,025	24.3	32.8	57.0	9.12	628	1.23	3.22	6.66	2.74
6	March 13-18	Fat 1.45 per cent., carbohydrate 2.1 per cent., protein 6.0 per cent., lime-water 5 per cent., 1½ dr. olive oil in day's food.....	1,050	16.7	28.6	61.6	9.85	563	1.19	3.64	7.97	3.35
7	March 18-27	So-called synthetic food, fat 1.45 per cent., carbohydrate 1.8 per cent., protein 6.0 per cent., 1½ dr. olive oil added to day's food; 120 c.c. breast milk March 26 and 210 c.c. March 26.	900	14.7	13.8	47.9	7.67	397	.327	2.49	6.13	2.77
			1,050	16.2	19.8	66.0	10.56	502	.574	3.44	7.66	2.77
			975	17.1	19.0	59.9	9.60	491	.515	2.98	7.54	3.44
			630	14.2	11.8	35.8	5.74	333	.242	1.98	4.34	2.08
			960	16.2	19.2	60.4	9.88	486	.463	3.22	6.66	2.93
			780	14.3	15.3	53.2	8.51	421	.434	2.82	6.27	2.66
			1,060	14.1	19.8	66.6	10.50	490	.642	3.49	7.76	3.76
			930	14.9	23.9	50.4	8.07	448	.400	2.74	6.29	2.92
			725	14.8	24.9	35.2	5.64	386	.300	1.90	4.08	1.99

Daily figures

CASE 3, FRANCIS D.

1	May 1	Fat 2.6 per cent., carbohydrate 4.5 per cent., protein 5.0 per cent., 2 dr. olive oil added to day's food	1,260	38.2	65.8	63.4	10.13	917	1.44	3.84	7.65	3.24
2	May 2-4	Fat 2.6 per cent., carbohydrate 3.5 per cent., protein 5.5 per cent., 2 dr. olive oil in day's food	1,260	38.0	46.0	71.4	11.42	877	1.49	4.12	9.34	3.71
3	May 4-19	Fat 2.6 per cent., carbohydrate 2.5 per cent., protein 6.0 per cent., 2 dr. olive oil in day's food. For method of making up this and two preceding formulæ see text	1,253	38.6	33.8	74.9	11.98	846	1.47	4.23	10.50	4.12
4	May 20-24	So-called synthetic food, fat 2.6 per cent., carbohydrate 1.8 per cent., protein 6.0 per cent., 2 dr. olive oil in day's food; 36 gm. lactose added to day's food May 23-24.	1,260	38.2	22.0	73.4	11.75	739	.253	3.75	8.65	3.36
			1,260	41.4	22.0	74.8	11.95	794	.360	3.95	9.95	4.17
			1,260	40.2	21.9	71.2	11.40	767	.256	3.62	9.11	3.69
			1,260	37.5	21.8	76.5	12.24	764	.359	3.62	9.60	3.85
			1,260	36.4	58.2	69.0	11.06	863	.167	3.61	7.99	3.39

Daily figures

* Estimated. † Average.

TABLE 3.—URINE CONSTITUENTS. AVERAGE DAILY VALUES

CASE 1, FRANCIS H.

Period	Dates	Volume, c.c.	Specific Gravity	Indican	Total Nitrogen, gm.	Ammonia Nitrogen, gm.	Ammonia Nit. Per cent. Total N.	Kreatinin Nitrogen, gm.	Kreatin Nitrogen, gm.	Inorg. Sulphates as H ₂ SO ₄ gm.	Etheral Sulphates as H ₂ SO ₄ gm.	Total Sulphates as H ₂ SO ₄ gm.	Chlorides as NaCl, gm.	Phosphates as P ₂ O ₅ gm.	Total Ash as Oxids, gm.	CaO, gm.
1	Sept. 14 to Oct. 3	426	1.010½	Gen. Negative	2.81	.240	8.5	.063	.023	.362	.123	.485	.817	.587	1.44	.079
2	Oct. 4-14	541	1.011	Neg. to High 10+	3.18	.118	3.7	.055	.011	.472	.131	.603	1.179	.635	2.72
3	Oct. 16-19	547	1.013	Negative	4.66	.152	3.2	.043	.047	.722	.122	.844	1.549	.731	3.39
4	Oct. 20-24	663	1.011	Negative	4.29	.073	1.7	.050	.078	.772	.080	.852	1.894	.729	4.45	.673
5	Oct. 25-29	703	1.011	Faint trace or neg.	4.78	.132	2.8	.042	.108	.695	.139	.834	1.791	.577	2.48
6	Oct. 31 to Nov. 6	488	1.018	Neg. or small trace	7.45	.342	4.6	.064	.055	1.078	.133	1.211	1.392	.832	3.21	.124
7	Nov. 14-16	475	1.016	Nearly negative	5.36	.158	3.0	.075	.008	.747	.188	.935	.806	.612	2.84
8	Nov. 16-21	550	1.012	Faint trace	5.30	.137	2.6	.071	.025	.671	.219	.890	.323	.636	1.69
		490	1.016	Faint trace	7.52	.178	2.4	.070	.059	1.129	.040	1.169	0	.639	1.65
		530	1.016	Trace	8.76	.279	3.2	.074	.008	1.122	.172	1.294	0	.780	1.59
		475	1.018	8-10	9.34	.326	3.4	.070	.025	.798	.558	1.356	0	.722	1.33
		350	1.019	16-20	7.36	.340	4.6	.081	.004	1.22	.165	1.385	0	.717	1.44
9	Dec. 12-16	514*	1.013*	Negative	3.35	.189	5.7	.048	.029	.523	.087	.610	1.53	.516	3.45	2.30*
	16-20	3.08	.187	5.7	.041	.008	.492	.055	.547	1.55	.757	4.31
	20-23	3.30	.158	4.8	.041	.042	.538	.080	.618	1.98	.566	4.07
10	Dec. 26 to Jan. 1	255	1.021*	Negative	3.70	.110	3.0	.044	.010	.632	.045	.677	.513	.582	2.61	.028*
		330	Large trace	6.65	.337	5.1	.055	.023	.904	.062	.966	.292	.747	1.77
		430	Trace	7.98	.344	4.3	.043	.020	.982	.019	1.001	.066	.525	1.52
		410	Faint trace	9.10	.327	3.6	.044	.0	1.185	.017	1.202	0	.865	1.31
		390	8-10	8.80	.405	4.6	.054	.027	1.124	.011	1.135	0	.642	1.72
		355	Trace	7.10	†047	1.185	.094	1.279	0	.686	1.77

TABLE 4.—COMPOSITION OF FECES. AVERAGE DAILY VALUES

CASE 1, FRANCIS H.

Period	Dates	Dried Weight, gm.	Dried Weight, per cent. of Moist.	Water in Feces, c.c.	Total Nitrogen, gm.	Total Nitrogen, %	Chlorid as NaCl, gm.	Phosphates as P ₂ O ₅ , gm.	Total Ash as Oxids, gm.	Total Ash % of Dried Weight	CaO, gm.	Total Fat, gm.	Total Fat, per cent. Dried Weight	Neutral Fat, gm.	Neutral Fat per cent. Total Fat	Free Fatty Acids, gm.	Fatty Acids per cent. Total Fat	Soap Fat, gm.	Soap Fat, per cent. Total Fat	Total Acidity per 100 gm. Dried Wt. N/10 NaOH	Volatile Acids, 24 Hours, c.c. N/10 NaOH	Volatile Acids per 100 gm. Dried Wt.	
1	Sept. 14 to Oct. 3	19.9	7.8	251	.782	4.0	.60	.92	3.98	20.0	1.28	6.96	34.7	4.72	66.2	1.18	16.8	1.06	17.0	181.6	903	118.6	639
2	Oct. 4-14	15.4	8.0	191	.707	4.6	.49	.80	4.56	29.6	1.34	4.61	29.5	2.94	63.6	.80	16.1	.87	20.3	119.9	779	137.3	907
3	Oct. 16-19	16.8	8.4	195	.922	5.5	.19	1.53	5.93	35.4	2.33	.43	3.9	.43	100.	133.3	799	110.0	658
4	Oct. 20-24	12.4	8.9	128	.587	4.7	.23	1.08	4.07	32.8	1.44	1.77	14.2	1.30	72.0	.25	16.2	.22	11.8	93.1	752	112.8	872
5	Oct. 25-29	7.7	16.2	40	.340	4.4	.05	0	2.87	37.0	1.27	1.23	15.6	.60	50.7	.12	7.9	.51	41.4	13.3	169	68.9	902
6	Oct 31 to Nov. 6	16.6	16.5	88	.663	4.0	.09	1.89	6.06	36.4	2.73	3.75	22.8	1.08	29.6	.14	4.3	2.53	66.1	25.6	148	128.0	757
7	Nov. 14-16	13.5	18.0	73	.594	4.4	.02	1.47	4.90	36.2	1.96	2.15	17.3	.65	27.6	.13	6.7	1.37	65.7	40.3	148	125.5	927
8	Nov. 16-21	16.0	13.7	95	.547	3.6	.17	1.87*	6.05	40.3	2.62*	2.72	18.1	1.38	50.8	.03	2	1.31	48.1	52.6	351	132.0	812
9	Dec. 12-16	11.7	21.0	44	.436	2.9	.02	4.66	39.8	4.53	38.6	.88	19.4	.15	3.1	3.50	77.5	76.3	65	93.5	797
		15.4	24.4	48	.443	2.9	.02	5.05	32.8	6.82	44.2	1.81	26.5	.63	9.3	4.38	64.2	19.0	123	148.5	964
		9.6	32.7	20	.296	3.1	0	3.18	33.2	4.16	43.4	.87	20.9	.40	9.7	2.89	69.4	8.9	93	53.9	662
		35.6	92.9	120	.856	2.4	0	10.85	30.6	19.20	54.0	6.16	32.0	.96	5.0	12.08	63.0	78.0	219	240.8	628
10	Dec. 26 to Jan. 1	12.9	11.7	99	.609	4.7	.11*	1.34*	3.49	26.9	1.91*	2.29	17.8	1.60	70.2	.35	15.4	.34	14.4	71.8	551	130.9	1,012
		12.5	8.2	142	.511	4.1	4.58	36.5	2.06	16.4	1.55	73.5	.48	24.9	.03	1.6	84.2	666	114.6	931
		11.8	11.1	96	.502	4.3	3.62	30.9	2.15	18.1	1.05	49.0	.43	18.4	.66	32.6	59.4	505	117.4	1,015
		16.1	14.6	18	.207	6.8	.08*	1.88*	.80	26.3	3.55*	.88	29.0	.42	48.0	.22	24.8	.24	27.2	6.7	218	106.2	3,490
11	Dec. 26 to Jan. 1	18.5	20.8	63	.807	4.9	5.38	32.7	2.75	16.7	1.20	43.7	.26	9.6	1.29	46.7	23.1	140	137.8	838
		20.0	15.3	111	.960	4.8	7.07	35.4	3.46	17.3	2.46	71.1	0	0	1.00	28.9	21.2	106	188.0	943
		12.0	15.4	66	.616	5.1	3.68	30.8	2.22	18.6	.90	40.3	0	0	1.32	59.7	32.5	272	118.0	988
		25.5	18.1	116	1.188	4.7	8.83	34.6	5.72	22.4	2.62	44.2	.59	10.3	2.61	45.5	61.1	239	183.0	718
12	Daily Figures	22.9	20.3	90	.897	3.9	5.72	25.0	8.02	35.0	5.99	74.9	2.03	25.1	0	0	100.8	440	166.5	728

CASE 2, JACOB S.

	1	2	3	4	5	6	7	Feb. 27-29	Feb. 29 to March 4	March 4-7	March 7-10	March 10-13	March 13-18	March 18-27	Daily Figures															
								11.6	15.9	62	.672	5.8	.04	1.25	3.35	28.9	1.58	1.53	18.1	.70	45.4	.58	37.8	.26	16.8	51.4	442	99.0	853	
								8.7	21.2	32	.506	5.8	.02	1.13	2.54	29.4	1.42	1.45	16.7	.73	50.3	.02	1.4	.70	48.3	22.0	254	92.6	1,068	
								16.4	14.8	89	.855	5.6	.06	1.66	4.12	26.8	2.22	3.56	23.2	1.79	50.2	.97	27.1	.81	22.7	77.4	504	136.6	883	
								10.8	15.5	59	.685	6.4	.12	1.55	3.22	29.8	1.75	.74	6.8	.45	60.8	0	0	.29	39.2	33.1	307	109.0	1,011	
								9.8	26.9	27	.546	5.6	.05	1.61	3.41	34.7	1.82	.73	7.4	.30	41.1	.07	9.6	.36	49.3	3.4	35	93.3	951	
								11.5	31.4	25	.576	5.0	.04	1.81	4.18	36.4	2.52	1.28	11.1	.42	32.8	0	0	.86	67.2	-3.6	-31	112.2	975	
								9.2	29.1	23	.450	4.9	.03	1.58	3.67	39.7	1.98	.83	9.0	.14	16.7	0	0	.69	83.3	-5.5	-60	73.9	801	
								5.2	33.8	10	.284	5.0	.01	.82	2.12	40.5	1.15	.15	2.9	.12	75.9	0	0	.04	24.1	4.8	-91	119.0	2,275	
								8.6	32.4	18	.430	5.0	.03	1.46	3.55	41.3	1.88	1.16	13.5	.27	23.0	.06	5.2	.83	71.8	0	0	104.0	1,213	
								46.7	21.6	170	2.519	5.4	.17	4.66	11.25	24.1	6.22	10.84	23.2	7.66	70.7	.14	1.3	3.04	28.0	168.3	360	336.0	719	
								28.1	16.9	138	2.454	8.7	.17	1.92	3.86	13.7	2.06	5.04	17.9	4.98	98.9	.06	1.1	0	0	183.6	652	184.0	548	
								26.8	13.9	166	2.411	9.0	.25	2.07	4.55	17.0	2.60	5.16	19.3	4.76	92.2	0	0	.40	7.8	245.0	916	177.2	662	
								21.4	13.5	137	1.675	7.8	.27	1.62	3.56	16.7	1.90	3.33	15.6	3.05	91.7	.28	8.3	0	0	120.0	562	168.8	790	
								29.4	13.3	133	2.233	7.6	.51	2.10	4.89	14.6	2.32	5.97	20.2	5.41	90.9	0	0	.59	9.4	184.5	927	154.4	524	
								* Average.	20.4	13.3	133	2.233	7.3	.51	2.10	4.89	14.6	2.32	5.97	20.2	5.41	90.9	0	0	.59	9.4	184.5	927	154.4	524

CASE 3, FRANCIS D.

	Daily Figures																							
1	May 1	20.2	18.4	90	.785	3.9	.10	.88	3.54	17.5	2.34	9.53	47.1	1.46	15.2	.44	4.7	7.63	80.1	40.5	200	162.4	803	
2	May 2-4	16.4	17.5	72	.659	3.7	.10	.85	3.34	21.6	1.87	6.31	40.9	1.54	24.4	.05	.7	4.72	74.9	26.6	173	203.0	1,318	
3	May 4-19	17.8	13.5	114	.694	3.9	.20	1.49	4.87	27.3	2.73	5.27	29.6	1.01	19.2	.07	1.3	4.19	79.5	29.6	166	131.8	740	
4	May 20-24	13.8	12.3	98	.626	4.6	.27	1.30	3.81	27.7	2.18	4.47	32.5	1.22	27.4	0	0	3.25	72.6	23.8	173	124.5	907	
		12.1	13.2	79	.605	5.0	.18	.86	2.42	20.1	1.26	4.20	34.8	1.79	42.6	.59	14.1	1.82	43.3	50.3	417	125.0	1,038	
		27.3	11.0	220	1.470	5.4	.62	1.98	6.06	22.2	3.25	9.30	33.6	4.34	46.7	3.99	42.9	.97	10.4	139.0	509	320.0	1,173	
		17.9	9.3	174	1.013	5.7	.75	1.11	3.57	20.0	1.78	5.42	30.3	2.70	49.8	.99	18.2	1.73	32.0	111.1	623	182.8	1,023	
		25.9	11.4	201	1.422	5.5	.46	1.54	4.48	17.3	2.14	6.91	26.7	4.50	65.2	0	0	2.41	34.8	163.0	631	204.0	789	

DESCRIPTION OF FECES

CASE 1, FRANCIS H.

1. Sept. 14-Oct. 3.—Thin, generally very watery, containing fat curds and few small hard curds, greenish-yellow, sometimes foamy; 8-12 stools daily.
2. Oct. 4-14.—Becoming more solid than in Period 1, more finely granular, 7-9 stools daily.
3. Oct. 16-19.—Orange-yellow, pasty or watery, containing hard curds and considerable mucus; 11-13 stools daily.
4. Oct. 20-24.—Watery or pasty, smooth and finely granular, containing small fat and protein curds, less mucus than in Period 3; 8-10 stools daily.
5. Oct. 25-29.—Mostly formed but soft, yellow-gray, smooth; 3-4 stools daily.
6. Oct. 31-Nov. 6.—Mostly formed, smooth, harder than in Period 5, portions watery or pasty, granular; 4-6 stools daily.
7. Nov. 14-16.—About as in Period 6; 4-5 stools daily.
8. Nov. 16-21.—After first day formed, hard and dry, containing fragments of hard curds; 3-6 stools daily.
9. Dec. 12-23.—Pasty or watery, containing fat curds, hard curds, and mucus, acid and rancid; 4-10 stools daily; more solid during last three days with less mucus.
10. Dec. 26-Jan. 1.—At first formed and semi-formed, rather soft and mealy, becoming hard and dry. After castor-oil was given largely watery and pasty, with small hard curds; 4-7 stools daily.

CASE 2, JACOB S.

1. Feb. 27-29.—Pasty, slightly formed, partly fluid, granular with fat curds, partly greenish; 4 stools daily.
2. Feb. 29-March 4.—Mostly formed, yellow-gray, smooth; 1-5 stools daily.
3. March 4-7.—More watery than in Period 2, foul, partly greenish, small part formed, 2-5 stools daily.
4. March 7-10.—As in preceding period, but generally more formed; 2-3 stools daily.
5. March 10-13.—Formed and hard; foul; 3-6 stools daily.
6. March 13-18.—As in preceding period, often with traces of blood; 3-7 stools daily.
7. March 18-27.—As in preceding period; 2-4 stools daily, until after castor-oil was given, then thin, pasty and watery, containing fragments of hard curds and mucus, generally greenish; 7-8 stools daily.

CASE 3, FRANCIS D.

1. May 1.—Formed, smooth, portion dry and hard, larger part soft, yellow-gray, 4 stools.
2. May 2-4.—As in Period 1; 1-4 stools daily.
3. May 4-19.—For first six days as in Periods 1 and 2, after that larger part thinner and less formed, 1-4 stools daily.
4. May 20-24.—Mostly watery and pasty, containing hard curds and often mucus, in increasing amount, partly greenish; about 3 stools daily.

TABLE 5.—BALANCES. AVERAGE DAILY VALUES

CASE 1, FRANCIS H.

Period	Dates	Total Nitrogen Retained, gm.	Nitrogen Retained, per cent. Intake,	Nitrogen Absorbed, per cent. Intake,	Total Fat Absorbed, gm.	Fat Absorbed, per cent. of Intake	Chlorid as NaCl Retained, gm.	Phosphates as P ₂ O ₅ Retained, gm.	Total Ash as Oxids Retained, gm.	CaO Retained, gm.	Gain or Loss in Body Weight, gm.	Weight Beg. and End of Period, gm.
1	Sept. 14 to Oct. 3	+1.17	24.5	29.4	83.5	+25.5	78.6	+1.07	+2.04	+1.19	+ 11.7	4,330
2	Oct. 4-14	+ .85	14.4	17.1	84.7	+29.0	86.5	+1.12	+ .32	+1.37	+ 4.6	4,553
3	Oct. 16-19	+1.03	15.6	18.1	86.2	0	+ .51	+ .54	+1.32	+ 25.7	4,683
4	Oct. 20-24	+ .69	12.4	13.9	89.6	+18.2	91.0	+ .59	+ .36	+ .90	— 23.3	4,781
5	Oct. 25-29	+ .80	10.4	11.1	94.1	+21.8	94.8	+1.63	+2.36	+1.53	+ 55.3	4,868
6	Oct 31 to Nov. 6	+3.01	27.0	28.7	94.2	+40.5	91.6	+1.28	+3.86	— .33	+ 64.8	4,884
7	Nov. 14-16	+1.99	25.1	27.1	92.7	+41.3	95.0	+1.06	+2.54	+ .76	+ 10.5	4,791
8	Nov. 16-21	+5.82 +2.58 +3.28 +1.30 —2.32	49.1 24.7 26.3 11.9	51.4 25.5 27.3 12.3	95.3 96.7 96.5 97.3 84.9	+29.1 +32.1 +32.9 +29.6 — 3.5	91.5 87.9 82.8 87.7	+1.027*	+3.97 +4.27 +4.98 +5.35 —6.82	+ .75*	+ 47.0 + 1.0 + 72.0 — 70.0 —497.0	5,016 5,063 5,084 5,136 5,066
9	Dec. 12-16	+1.00	20.2	23.1	87.9	+23.9	91.4	+ .61	+ .05	— .35*	— 30.3	4,569
	16-20	+1.41	28.2	31.4	89.9	+18.6	90.4	+ .37	+6.05	+ 50.3	5,206
	20-23	+1.16	23.3	26.0	90.1	+27.8	93.1	+ .56	+1.22	+ 9.0	5,085
10	Dec. 26 to Jan. 1	+1.08 +2.73 +2.69 +3.48 +2.51 —6.06	21.8 26.8 23.1 26.4 20.1	22.7 29.2 25.2 27.7 22.2	96.1 92.1 91.8 95.3 90.6 53.8	+ 9.72 +25.2 +22.6 +21.6 +17.8 — 4.3	91.6 90.2 90.3 90.6 75.7	+ .385*	+1.37 + .30 +1.90 +4.95 +1.23 —5.88	— .40*	—276.0 +226.0 + 27.0 — 33.0 +109.0 —697.0	5,313 5,265 4,989 5,215 5,242 5,209 5,318 4,621

* Average.

CASE 2, JACOB S.

1	Feb. 27-29	+1.89	35.1	40.0	87.7	+25.1	94.2	+22	+ .42	-1.18	+ .38	+ 92.0	3,968
2	Feb. 29 to March 4	+1.62	25.0	27.0	92.4	+25.6	94.8	+ .08	+ .83	+ .75	+ .86	+ 14.0	4,151
3	March 4-7	+1.17	17.1	19.5	87.6	+25.5	87.9	+1.31	+ .268	- .26	+ .04	- 6.0	4,208
4	March 7-10	+1.77	21.3	23.2	91.8	+24.2	97.2	+ .437	+ .78	+1.20	+ .61	+ 29.0	4,191
5	March 10-13	+2.13	23.6	25.1	94.0	+23.6	97.1	+1.28	+1.01	+1.63	+ .89	+ 16.0	4,278
6	March 13-18	+1.62	16.4	17.4	94.2	+15.4	92.3	+ .029	+1.08	+1.74	+ .78	+ 19.0	4,326
7	March 18-27	+1.22	15.9	16.9	94.2	+13.8	94.5	- .42	+ .31	+ .86	+ .80	- 75.0	4,423
Daily Figures		+3.98	37.7	38.7	97.8	+15.1	99.0	+28	+2.17	+ 60.0	4,348
		+1.34	14.0	14.6	95.6	+15.9	93.4	+1.14	+ .77	+2.34	+1.56	+ 19.0	4,408
		-3.20	66.1	+3.4	23.6	- .39	-3.29	-8.17	-4.11	-313.0	4,389
		+1.98	20.5	27.4	74.9	+11.1	68.6	+1.11	+ .65	+1.78	+ .88	- 21.0	4,076
		- .15	71.7	+9.11	63.8	+1.10	+ .20	+ .67	+ .04	- 35.0	4,055
		+3.66	34.8	41.4	84.0	+10.8	76.4	+ .29	+1.46	+3.28	+1.86	+ 21.0	4,020
		+ .15	1.9	2.6	72.4	+8.9	60.0	- .20	+ .20	+ .43	+ .30	- 46.0	4,041
		- .90	70.2	+11.4	77.4	- .08	+ .09	+ .49	+ .34	-127.0	3,985
													3,868

CASE 3, FRANCIS D.

1	May 1	+2.96	29.2	31.7	92.2	+28.6	75.2	+ .768	+1.53	+1.58	+ .80	+147.0	4,725
2	May 2-4	+3.32	29.0	30.5	95.2	+31.7	83.5	+ .505	+1.74	+3.16	+1.74	- 41.0	4,872
3	May 4-19	+3.42	28.5	30.3	94.3	+33.3	86.4	+ .502	+1.42	+3.10	+1.29	+ 18.0	4,790
4	May 20-24	+3.47	29.5	31.2	94.7	+31.7	87.7	- .192	+1.32	+2.68	+1.18	+ 71.0	5,077
Daily Figures		+6.56	54.9	57.8	94.9	+37.2	89.8	+1.61	+2.34	+6.07	+2.90	- 61.0	5,148
		+2.40	21.1	24.2	87.1	+30.9	76.9	- .360	+ .52	+1.04	+ .44	- 83.0	5,087
		+2.77	22.6	24.6	91.8	+32.1	85.7	- .390	+1.66	+3.51	+2.07	- 8.0	5,004
		+2.27	20.5	23.6	87.1	+29.5	81.1	- .295	+ .98	+1.38	+1.25	-203.0	4,996
													4,793

TABLE 6.—PRELIMINARY OBSERVATIONS ON CASE 3

Period	Dates	Composition of Food	Body Weight, gm.	Volume Urine, c.c.	Specific Gravity of Urine	Indican in Urine	Intake Chlorids as NaCl, gm.	Chlorids as NaCl in Urine, gm.	Phosphates as P_2O_5 in Urine, gm.
1	January 5-6	Fat 1.5 per cent., carbohydrate 2.2 per cent.	3,882	630	1.009	Faint trace	1.46†	.895	.529
	6-7	Protein 3.4 per cent.	4,076	490	Negative608	.586
	7-8		4,027	505	Faint trace869	.539
2	8-9	Fat 1.6 per cent., carbohydrate 2.3 per cent.	3,957	355*	Faint trace	1.40†	.693	.354
	9-10	Protein 4.0 per cent.	4,102	570	Faint trace775	.405
	10-11		4,090	500	Faint trace770	.406
3	11-12	Fat 1.7 per cent., carbohydrate 2.0 per cent.	4,114	410	1.013	Considerable	1.35†	.372	.416
	12-13	Protein 4.6 per cent.	4,051	390	1.013	Considerable924	.371
	13-14		3,998	370	1.014	Considerable	1.314	.357
4	14-15	Fat 1.7 per cent., carbohydrate 2.1 per cent., protein 5.1 per cent.	3,948	340	Considerable	1.19	.565	.346
	15-16	Fat 1.8 per cent., carbohydrate 2.3 per cent.	3,961	295	1.019	Trace	1.27†	.541	.266
	16-17	Protein 5.5 per cent.	3,944	295	1.015	Faint trace506	.229
5	17-18		3,914	400	1.019	Trace570	.467
	18-19	Fat 1.5 per cent., carbohydrate 2.4 per cent.	4,034	420	1.019	Small trace	1.31†	.422	.449
	19-20	Protein 6.0 per cent.	4,059	280	1.021	Considerable689	.348
6	20-21		4,093	440	1.021	Negative	1.142	.469
	21-22		4,026	250*	1.020	Considerable695	.318
	22-23	Synthetic food, 1.8 per cent., carbohydrate 1.8 per cent.	4,045	490	1.016	6-10 per cent.	.579†	.450	.406
7	23-24	Protein 5.9 per cent.	4,090	480	1.016	20-25 per cent.085	.535
	24-25		3,980	520	1.014	Small trace	0	.540
	25-26		4,026	490	1.018	10-15 per cent.572
	26-27		3,939

*Loss. †Average.

A BRIEF REPORT OF AN EPIDEMIC OF SORE THROAT
WITH INVOLVEMENT OF THE CER-
VICAL LYMPH-NODES *

JOHN RUHRAH, M.D.

BALTIMORE

There have been reported from time to time in European cities certain epidemics more or less associated with the milk-supply. Some of these epidemics have had a clinical picture which is more or less characteristic and which has been called by the English observers septic sore throat. The report of the United States Public Health Service records eight epidemics that occurred in England, the first in 1881 and the last in 1905. Bacteriologic examinations were not made in all these, but in the cases so studied the streptococcus was found. In seven of the eight epidemics one, or more, cows was discovered suffering from mastitis or from an eruption of the udder. In 1908 there was a remarkable epidemic which occurred at Christiania; this was found to be due to one milk-supply, and one cow was discovered with a diseased udder. From the cow there was isolated a streptococcus which was found in every way identical with the streptococci obtained from the patients suffering with the disease. The methods in use at that time for differentiating the varieties of streptococci were not as good as at present and even our present methods leave much to be desired.

Similar epidemics have been reported in other foreign cities. The first outbreak of this kind in the United States with which I am familiar occurred in Boston in 1911. This epidemic was one of unusual severity, affected chiefly adults, and was finally traced to one of the largest and best controlled dairies supplying milk in Boston. This year, in the month of February, a similar infection was noted and Dr. Mark Richardson, secretary of the Massachusetts State Board of Health, in a letter writes: "We found at a milk depot of this firm conditions which we thought explained it. At any rate we requested that all the milk from this special milk depot be pasteurized, and the epidemic promptly ceased."

A similar outbreak occurred at Concord, N. H., and Davis and Rosenow reported a large number of cases that occurred in Chicago.

In Baltimore the epidemic began early in January. Curiously enough, one or two cases presenting exactly the same clinical picture were

*Read at the meeting of the American Pediatric Society, Hot Springs, Va., May, 1912.

observed in December. The cases increased throughout February and in the third and fourth weeks became very numerous. After the first three weeks of March were over very few of the typical cases were noted, although there was a large number of cases of sore throat from which streptococci could easily be isolated, but which were free from the complications that characterized the epidemic.

Dr. Louis Hamburger was one of the first to recognize the epidemic as milk-borne, and the subject of the disease was talked over at a meeting called at his suggestion. The results of his experiences were charted and they showed conclusively that a great number of people were using milk from one of the largest dairies in the city. For example, in two homes for trained nurses one used milk from the suspected dairy and showed a percentage of 71.4 of the inmates suffering during the epidemic from some form of sore throat; this is in striking contrast with 8.3 per cent. in the other home which was using milk from another dairy. In sixteen fatal cases it was found that fourteen used milk from the suspected dairy, and that in two the milk-supply was unknown. Both of these unknown cases occurred in adults, one before the milk-supply was suspected, and the other was in a hospital patient who was too ill to be interrogated.

Another method of studying the relation of the disease to the milk-supply was by taking a group of households using the infected milk and a similar group, taken at random, using other milk, the only requirement in the cases so taken being that the households should contain two or more children. The results were about the same as that shown in the nurses' homes.

Subsequently the disease was studied by Dr. Frost of the United States Public Health Service, and the results of his investigations will be published in a separate paper. He found, however, that in about 80 per cent. of the cases which occurred from the middle of February to the middle of March the patients were using milk from a suspected dairy. He was able to find some 600 undoubted cases of the disease, but this represented only about one-third or one-fourth, or even a smaller percentage, of the actual number of cases which occurred during the epidemic. In these 600 odd cases there were twenty-eight fatalities and twenty-two of these had used milk from the suspected dairy.

An interesting point in relation to the suspected dairy in the Baltimore epidemic was that previous to the epidemic the flash method of pasteurization had been used. Wishing to make some repairs and improvements in the pasteurizing room, pasteurization was stopped during a considerable portion of the time in January and February and in the first part of March. The weather during this time was extremely cold and it was thought that the repairs and improvements could be made more safely at this time than at any other season of the year. Following

the announcement that the epidemic was caused by milk a holding pasteurizer was installed and after this the epidemic promptly ceased. About this time, however, it should be borne in mind that the public was repeatedly warned through the daily papers to boil the milk, and a very large number of people using milk followed this^e direction and this undoubtedly had much to do with the prompt cessation of the epidemic.

The Baltimore epidemic differed somewhat from the others which have been described, in that children were very largely affected, fully 50 per cent. of the cases occurring in early childhood. Cases were noted in children as young as 4 months, and Dr. Hamburger had one case at 65 years of age, and he also stated that he knew of one case, which was not included in his series of cases, in which the patient was 86 years of age. In my own cases, all in children, almost all of them occurred between the ages of 12 and 24 months.

There seems to be little doubt that the disease was originally derived from using contaminated milk, but once having been started it was possible to have the disease transmitted in the ordinary ways. It frequently happened that all the members of a household would be affected, but for the most part the adults escaped with light attacks. In a number of instances nurses in constant attendance on the children became affected and had typical attacks. In one instance a cat which drank freely from the infected milk was affected very much in the same way that children were, that is, with an angina and enlargement of the cervical lymph-nodes.

Bacteriology.—I am indebted to Dr. Standish McCleary for the following information: The organism, frequently in pure cultures, which was seen in smears made from these patients, was a diplococcus with a distinct capsule, easily demonstrable with the usual capsular strains. The diplococcus was Gram-positive. When grown on all mediums this capsule disappears but returns after passage through mice. When cultivated the organism takes the form of a streptococcus in short chains in which the diplococcus arrangement is preserved. Occasionally tetrads are seen. On slant agar a thin, slightly moist dewlike colony is obtained. Hemolysis occurs on blood-agar. Litmus milk is acidulated and coagulated and broth is rendered turbid. Lactose and saccharose are fermented but not inulin. The thermal death point in milk is 54 C. at an exposure of twenty minutes. The organism is found in the pus of the otitis which occurred so frequently, and also in the suppurating lymph-nodes, which were not frequent. In some cases the pneumococcus was obtained from the throat, sometimes in pure culture.

The Clinical History.—There are four classes of cases met with—mild cases, cases of average severity, severe cases, and cases of unusual intensity, usually owing to some severe complication occurring at the onset.

The mild cases were for the most part in adults and many were not sufficiently ill to go to bed; very few of these came under my personal observation. They were characterized by an angina of mild intensity, and for a day or two slight enlargement of the cervical lymph-nodes. There was slight fever, headache and general malaise. These symptoms persisted for several days and then usually from two to three weeks would elapse before the patient felt quite well, and many complained of slight recurrence of the symptoms, lasting twenty-four hours or more. There were some mild cases in children; by far the greatest number, however, presented the same clinical picture. There was sudden onset with fever, and occasionally a convulsion; the temperature varied from 101 to 104 or 105 F., and there was considerable prostration. At the outset the only physical sign of any importance was the general redness of the pharynx and pillars of the fauces; this was usually a dusky red and at some places there were slight patches of exudation, particularly on the tonsils. This exudation could easily be mistaken for diphtheria but was not nearly so adherent, and much of it consisted of pus which could easily be wiped off. In other cases there was the typical appearance of a tonsillitis, the crypts being filled with a more or less hard and purulent material. Children old enough complained of pain usually located in the head, neck or abdomen. After two or three days there was marked swelling of the lymph-nodes at the angle of the jaw. These were almost always on both sides and varied in size from a hazel nut to a pigeon's egg, or even larger. There was more or less exudate into the subcutaneous tissues, and these swellings were painful and tender to the touch; they persisted for two or three weeks and gradually subsided, in most instances leaving the nodes normal in size or very slightly enlarged. The fever and prostration varied greatly, the mild cases lasting a week to ten days; some of the more severe cases continued as long as two weeks, and sometimes longer.

The severe cases came on with great intensity, usually either with a chill, or more commonly with a convulsion, the temperature rising rapidly to 106 or 107 F., and sometimes even higher. The appearance of these children was very alarming, the pulse was rapid and weak and the respirations irregular and shallow. There were marked pallor and more or less cyanosis; in some there were marked vomiting and sometimes diarrhea. After a day or two the lymph-nodes at the angle of the jaw enlarged and usually this was coexistent with an improvement in the general condition. In many of the severe cases there were complications as noted below.

The worst class of cases either started with very severe symptoms or sometimes these symptoms came on two or three days later. In these cases there was no enlargement of the lymph-nodes, or the enlargement

was slight, and the general clinical picture was that of a septicemia with very high, irregular temperature, great prostration, usually numerous complications and death. Certain other cases were characterized by the appearance of a peritonitis which was apparently only a complication in the course of the septicemia. The fatal cases are striking, the usual history being of a child in perfect health taken with a convulsion and high fever and slight redness of the throat; the child was either comatose or partially so; there were generally vomiting and diarrhea and distention of the abdomen, which later became very tender, and then a considerable rigidity of the muscles developed; within forty-eight or seventy-two hours after the onset the child would die, sometimes from failure of respiration, occasionally from failure of the heart.

Complications.—The complications attending this disease were remarkable for their number and their intensity; most common of all was the inflammation of the middle ear, which occurred in from 30 to 40 per cent. of the cases. Next to this were irregular swellings, sometimes suggesting an edema, at other times suggesting abscess formation, although these swellings rarely suppurated. The swellings were most frequently noted about the throat over the epiglottis, or at the base of the tongue at the side, sometimes in the floor of the mouth, sometimes posteriorly in the pharynx, suggesting retropharyngeal abscess. Suppuration was not a very common thing in my experience, apart from the inflammation of the middle ear, and in only two instances did the lymph-nodes in the neck suppurate, and in one of these the suppuration evidently followed a retrotonsillar abscess. In one instance there was a retropharyngeal abscess, and in one other case numerous points of suppuration occurred apparently independent of the swollen nodes. Edema of the eyes, affecting both lids and the tissues about the orbit, was not uncommon, and this usually, although not always, was unilateral and accompanied with nothing more than a slight conjunctivitis with little or no discharge. Bronchitis was not uncommon, and quite a number of patients had pneumonia as a complication. Gastro-intestinal disturbances were also common, usually consisting of vomiting and a very irritable stomach, and later on a more or less intense diarrhea. In three cases there was an erysipelas, two occurring on the scalp and one on the face. These ran a typical erysipelas course and finally stopped suddenly. In some cases the joints were swollen, and in some others the tissues about the joints, the joints themselves remaining more or less free. In some cases there were petechiæ, and in others larger ecchymotic spots, and in one instance there occurred about the tenth day very large subcutaneous hemorrhages, as if there had been an actual rupture of some of the larger vessels and which suggested the rupture of the vessels which has been noted in experimental work in pneumococcus infections. In one instance the hemor-

rhages occupied both sides of the scalp, and also the arm from the wrist nearly to the shoulder, the swelling thus produced being larger than one would imagine was possible.

CONCLUSIONS

The lessons to be learned from this epidemic are as follows:

1. A streptococcus infection may be caused by infected milk, and this disease may be exceedingly severe and attended with numerous complications and fatalities.
2. Even in cold weather milk may be the source of the disease.
3. No matter how carefully raw milk is handled it may at times be a source of danger.
4. The milk supplied to cities should be pasteurized, and where by accident the dairy company cannot properly pasteurize its milk, it should be compelled to notify its consumers, so that they can either pasteurize or boil the milk.

EFFECTS OF COLD AIR ON BLOOD-PRESSURES OF
CHILDREN AND YOUNG ADULTS IN VARIOUS
STAGES OF TUBERCULOSIS *

B. RAYMOND HOOBLER, A.M., M.D.

NEW YORK

Through the work of many observers it has been definitely established as a clinical fact that the blood-pressure of patients with tuberculosis is reduced considerably below normal. Most of the observations on record, however, have been made on adults and but few on children. Strandgaard's¹ reports included a large number of children, but his figures were not given separately. Pottenger's² series included only four patients between 14 and 16 years, all of whom showed lower pressure than normal. Levy's³ cases reported but two children in very early stages, both of whom showed no change from normal. A large number of cases have been reported in which the ages of the children have not been given. There are, however, sufficient reports to show that the pressures of children are affected much as those of adults. Emerson⁴ has recently presented an exhaustive study and reviewed the various theories of causation of this hypotension. He concluded that "the causes of low blood-pressure in tuberculosis are probably, primarily, a toxic action on the vasomotor center in the medulla, allowing of a vasoparesis or stimulating an active vasodilatation, and secondarily, progressive cardiac atrophy or degeneration." It is evident, therefore, that in a disease in which the blood-pressure is so constantly lowered, one of the essential principles of treatment should be the combating of this lowered pressure.

Dec. 15, 1910, I presented to the medical section of the New York Academy of Medicine a preliminary report with charts, showing the effect of cold air on the blood-pressure of a young adult having incipient tuberculosis, an abstract of which appeared in *The Medical Record*, Jan. 28, 1911.

Since that time a series of blood-pressure observations, 150 in all, have been made on children and young adults in various stages of pulmonary tuberculosis. In general it may be stated that every case having

*Read in the Section on Diseases of Children of the American Medical Association at the Sixty-Third Annual Session held at Atlantic City, June, 1912.

1. Strandgaard: N. J. Hosp.-Tid., 1907, xv, 1041.

2. Pottenger: Arch. Int. Med., 1909, vi.

3. Levy: Beitr. z. klin. d. Tuberk., 1905, xiv, 99.

4. Emerson: Arch. Int. Med., 1911, vii, 441.

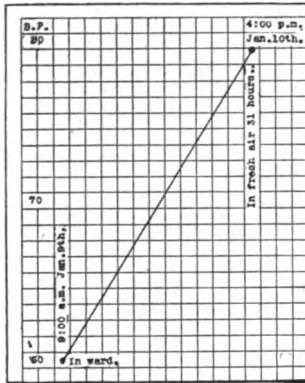


Chart 1

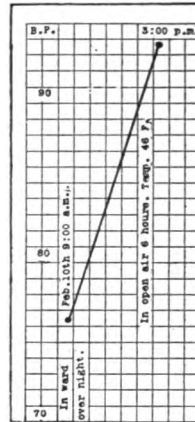


Chart 2

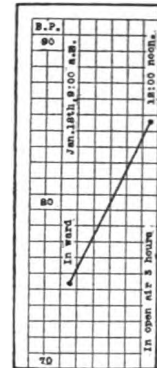


Chart 3

Chart 1.—Advanced case pulmonary tuberculosis. Girl aged 1 year. Febrile throughout entire illness. Died forty-five days after this observation. Chart shows exceedingly low pressure when in ward, with a rise of 20 mm. Hg after being in cold air for thirty-one hours.

Chart 2.—Advanced case of pulmonary tuberculosis. Boy of 1 year; admitted January 27, died February 13. Observations taken three days before death.

Chart 3.—Moderately advanced case pulmonary tuberculosis. J. F., boy, aged 2½ years. On day observations were made the child had a temperature varying from 100 to 102.5 F. The child was discharged improved after two months in the hospital. Chart shows a rise of 14 mm. Hg after being in cold air for three hours.

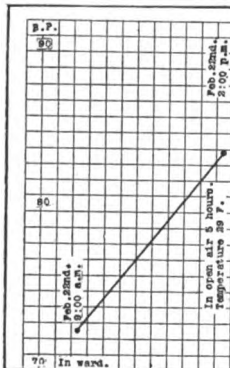


Chart 4

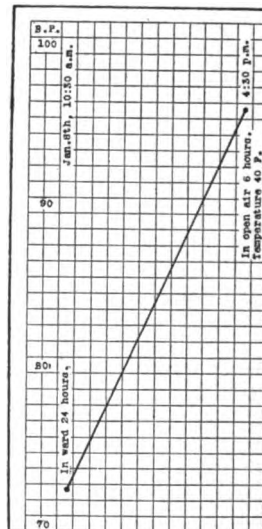


Chart 5

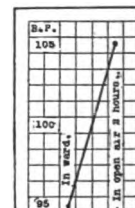


Chart 6

Chart 4.—Moderately advanced case of pulmonary tuberculosis. Girl of 3 years. Febrile throughout course; not improving.

Chart 5.—Incipient case of pulmonary tuberculosis. R. G., boy, aged 5 years; slight involvement at right apex; temperature below 100 F. Discharged improved 17 days after observations were taken.

Chart 6.—Incipient pulmonary tuberculosis. M. C. young adult, aged 16 years; slight involvement at right apex. Temperature below 101 F. Sent to mountains two days after observation. Chart shows a rise of 10 mm. Hg after being in the open air for two hours.

a definite pulmonary lesion showed a decrease in blood-pressure. When transferred from the ward or small room to the open air these patients all showed an increase in blood-pressure. This explains, to a large degree, the value of the outdoor treatment of tuberculosis and gives a very definite basis on which to urge this form of treatment.

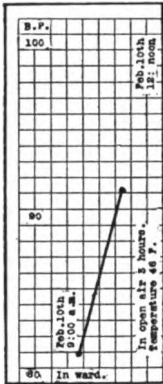


Chart 7

Chart 7.—No demonstrable lesion; von Pirquet reaction, positive. D. W., girl aged 2 years. Clinical diagnosis, rachitis; no demonstrable sign of tuberculosis. Chart shows but a slight rise in pressure when put in the open air.

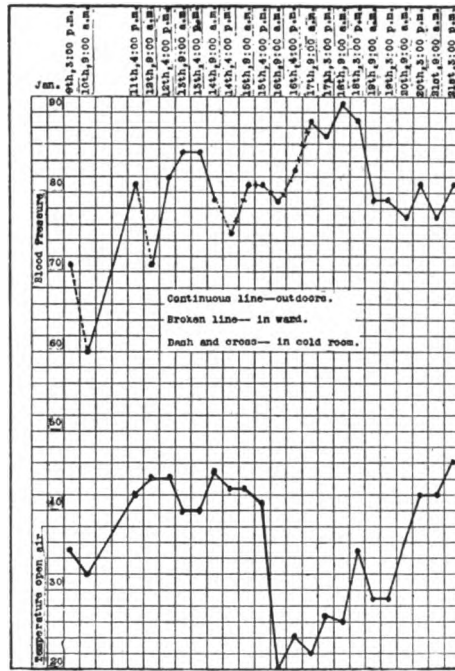


Chart 8

Chart 8.—Advanced case of pulmonary tuberculosis. Girl 1 year old was kept constantly under influence of cold air either in a cold room or out of doors for period of sixteen days, except on three very unpleasant days. Both blood-pressure and out door temperature are shown on the chart. It should be noted that the blood-pressure when in the ward varied from 60 to 70 mm. Hg and that through the influence of continuous residence in the cold air the pressure was maintained at an average of 80 mm. Hg, being about the normal pressure for a child of 1 year. It should be further noted that in periods of lowest temperature the blood-pressure rose the highest. It should also be noted that after several days in the open air when the child was brought into the ward the blood-pressure did not fall to as low a point or as much as before fresh cold air treatment was begun.

The charts presented are cases of advanced, moderately advanced and incipient pulmonary tuberculosis, also one which gave a positive von Pirquet reaction, but which had no demonstrable pulmonary lesion. (The charts with their legends are sufficiently clear to need no further discussion.)

SUMMARY

From a study of the foregoing charts it appears that:

1. Blood-pressure in children having tuberculosis is persistently low, as has been found to be the case in adults.
2. When a patient is transferred to the open air there is a gradual increase of blood-pressure within one or two hours.
3. If the patient is kept constantly in the open air the pressure is raised to well within the normal limits and sustained at that point as long as the patient remains in the open air.
4. The more advanced the case, the lower the pressure indoors, and the higher the rise when put in the open air.
5. After several days in the open air the blood-pressure does not fall as much when placed in ward as it did previous to outdoor treatment.

131 East 67th Street.

PAROXYSMAL HEMOGLOBINURIA *

REPORT OF A CASE IN A FEMALE CHILD; POSITIVE WASSERMANN IN CHILD
AND MOTHER

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Charpentier's treatise on the various types of hemoglobinuria is so concise and reviews the literature so thoroughly to the date of its publication that it would be futile to go over the details here. He describes paroxysmal hemoglobinuria as follows:

It usually attacks men (women are seldom affected) of a pale and sallow complexion, who may or may not have had some specific disease, such as malaria or syphilis, or who have a bad family history, in fact, whose vitality is from any cause lowered.

After exposure to cold the patient has rigors and feels ill. Soon after he passes dark colored urine which contains large quantities of hemoglobin but rarely blood corpuscles.

Holt says in the last edition of his book, page 602:

Paroxysmal hemoglobinuria occurs in childhood, although it is an extremely rare condition.

The subject is not mentioned in other American text-books on children's diseases. Pfaundler and Schlossman describe the disease but do not give the latest studies in regard to it.

Following Ehrlich's theories, Kretz and Eason in 1902, and Donath and Landsteiner in 1904, studied the blood of these patients and demonstrated the following:

First, that the blood-serum contains a complex hemolysin of amboceptor — complement nature.

Second, that this lysin can only act in the presence of this complement, that is, the serum may be rendered inactive by moderate heat and then reactivated by the addition of a small amount of some other serum which in itself is not hemolytic.

Third, this lysin must be chilled far below normal body temperature in order to become active, either in the body or in the test tube.

Fourth, this lysin is both autohemolytic and isohemolytic; that is, it destroys the red cells of the individual and also the red cells of other individuals of the same species.

*Read before the Medical Society of the County of Kings, N. Y., June 18, 1912.

Although syphilis has always been assigned as one of the principal causes of this symptom-complex, it is only since the general application of the Wassermann reaction that any accurate figures have been obtained. During the past two years I find records of thirty-four cases; in addition, R. A. Cooke reported a case in May at the Academy of Medicine, as yet unpublished. The case here reported seems to be the thirty-sixth. Some of the facts are as follows:

Reference	Age	Sex	Syphilis At Age of, Years,	First Attack of Hemoglobinuria, At Age of, Yrs.
.....
1.	64	M	48	60
2.	28	M	22	25
3.	48	M	Was	..
4.	48	M	?	40
5.	36	M	25	29
6.	34	M	24	33
6.	33	F	Was	33
7.	8	F	Congenital	5
7.	7	M	Congenital	5
7.	32	M	Congenital	24
8.	10	..	Congenital	5
9.	56	M	30	55
10.	4	M	Congenital	4
11.	30	F	?	25
12.	16	M	Congenital	..
12.	37	M	Acquired	..
12.	45	M	Acquired	..
12.	53	M	Acquired	..
12.	42	M	Acquired	..
12.	50	F	Acquired	..
12.	27	M	Acquired	..
12.	49	M	Acquired	..
12.	24	M	Acquired	..
12.	14	M	Congenital	..
12.	15	M	Congenital	..
12.	18	F	Congenital	..
12.	19	F	Congenital	..
12.	7	M	Congenital	..
12.	42	M	Congenital	..
12.	27	M	Acquired	..
12.	6	M	Congenital	..
12.	6	F	Congenital	..
12.	20	M	Congenital	..
12.	30	M	Acquired	..
14.	38	M	Congenital	23
15.	3	F	Congenital	2

These figures confirm the observation of the earlier writers that a large majority of the patients are males; in this series 27 males, 8 females, 1 unknown.

In the different age periods we find 23 cases over 20 years, 4 cases between 15 and 20 years, and 9 cases under 15 years. At first sight these facts seem to agree with Charpentier's statement that this is chiefly a disease of adults. As a matter of fact, however, the statistics are about what would be expected under the law of averages. That is, one-quarter of the cases are in early life as a late manifestation of congenital lues, one-eighth during adolescence and the others in adult life.

Of the total 30 cases, 17 had congenital syphilis, 15 acquired syphilis, 2 had positive Wassermann tests, type unknown, and in 2 the question of syphilis was not determined. This seems to indicate that hemoglobinuria is much more apt to follow congenital than acquired syphilis, but I have no accurate knowledge in regard to the relative frequency of the two types.

CASE REPORT

The case I desire to report is the following:

History.—L. C., female, aged 3 years and 4 months, a Syrian child born in Syria, was first seen, April 1, 1912. Both parents are living and apparently in good health. The mother is rather fat and was in the last month of pregnancy when first seen. The father is a thin nervous man with the typical Syrian physiognomy. The Wassermann test was negative. The mother was previously married and had two miscarriages. Her first husband died of "heart disease." There has also been one miscarriage since this child was born. There was positive Wassermann reaction. During the first week in May the mother gave birth to an apparently healthy boy, fat, skin healthy, no snuffles. At 2 weeks the baby had a slight cold in the head and diarrhea. It began to lose weight and had some desquamation on its hands and feet. At present—June 5, 1912—he has an enlarged liver, profound jaundice, bile in the urine and is falling rapidly, in spite of the use of calomel and mercuric chlorid. June 3 a Wassermann test was made but neither the test nor the control showed cytotoxicity, possibly on account of the large amount of bile in the blood serum.

The patient has always been well, according to the mother: that is, she has had no acute diseases. She was nursed for the usual period and developed normally during the first year although she had some diarrhea. She has always had a good appetite and is apt to be constipated. At 1 year and 10 months she had the first attack of "bloody urine" and has had them at varying intervals ever since, particularly during cold weather. The attacks come on after exposure to cold and are ushered in by definite chills—a very rare symptom in small children. The chill is followed by pain in the back, marked prostration and drowsiness and then the "bloody urine," without any bladder irritability.

Physical Examination.—The child has the typical Syrian features, is short and stocky, a fat little girl. She is very anemic and has some marginal blepharitis. There is very little evidence of rachitis although 80 per cent. of the Syrian children in this country seem to be markedly rachitic. Apparently the child is otherwise normal. There is no pain nor tenderness.

The history indicated some chronic infection in the urinary tract—tuberculous kidney—stone in the kidney—colon pyelonephritis. The fact that she was first attacked in Syria suggested the possibility of a bilharzia infection. Urotropin and water were prescribed and a sample of urine was requested. On the way home from my office she had another chill and in two hours I had a sample of dark red urine without any blood cells, which showed that it was not hematuria but hemoglobinuria. This was confirmed by a spectroscopic examination. A few hours later the urine was clear, with only a trace of albumin. The child was

placed in the Long Island College Hospital for greater convenience and Drs. Avery, White and Murray of the Hoagland Laboratory very kindly undertook the examination of the blood, and I am indebted to them for the chief interest of this paper. During the few days between the visit to my office and admission to the hospital the child had a number of attacks and the anemia was profound. Dr. Murray found the blood condition as follows:

Hemoglobin	45%
White cells	5,200
Red cells	3,200,000
Color index	0.7
Differential count:	
Polynuclears	35.4%
Lymphocytes	51.0%
Large mono. and transitionals	12.8%
Eosinophils	0.8%
One neutrophilic myelocyte. No erythroblasts.	

There was marked megalocytosis and polychromatophilia and moderate poikilocytosis. The Wassermann test was positive.

This indicated not only a profound anemia but also a marked degenerative condition of the red cells and an exhaustion of the organs of red cell production. Nevertheless the confinement in bed and the even temperature in the hospital promptly checked the cytolysis, and improvement was rapid. She was removed by the family at the end of two weeks and soon after developed German measles. In spite of this there were no more attacks, probably on account of the season of the year. May 29 the blood-examination was as follows:

Hemoglobin	70%
Red cells	4,200,000
White cells	8,400
Polynuclears	30.0%
Lymphocytes	55.0%
Eosinophils	1.8%
Large mononuclears	0.0%
Red cells normal in shape, size and staining.	

EXPERIMENTS IN HEMOLYSIS

The first attempt to get enough blood for hemolysis studies was not very satisfactory on account of the adipose tissue and the small size of the veins. Later I opened a vein in the foot and secured 10 c.c. With this serum a number of tests were made in which the results coincided with the reports of other observers. The two experiments demonstrating hemolysis were as follows:

The blood was allowed to clot and the clear serum was drawn off. Some of the red cells were then washed out of the clot and a 5 per cent. volumetric suspension of them was made in normal salt solution. In each of two test-tubes were put .25 c.c. of the serum and the same amount of the suspension of red cells. One of these tubes was packed in ice for half an hour, and then both were placed in the incubator at 37 C. for two hours. In the tube that had been chilled the red cells were completely destroyed; in the other tube they were not affected.

The second experiment was the same as the first except that the red cells were derived from a normal human being. Hemolysis was the same as in the first experiment. This second experiment shows that the old idea that the red cells in these patients are so diseased that they break down easily, is a mistake. It proves that the blood-serum contains some substance which unites with the red cells when the blood is sufficiently cooled, as in the superficial capillaries, and that the cells are then dissolved when they are again warmed in the interior circulation.

That there are two steps in the chemical process is shown by "inactivating" the serum by a temperature of 50 C. for twenty minutes; after which it will not destroy the red cells. If, however, a small amount of normal serum is added — which in itself has no cytolytic power — the hemolysis again occurs under the same conditions as before. In this particular case it was found that the serum became inactive after standing at room temperature for twenty-four hours, but it was readily reactivated by the addition of complement in the form of normal serum.

As this is merely a clinical report I will not take up the discussion of the many interesting biochemical problems involved. Many of them have been studied by Moss, Kumagai and Cooke, and others have not yet been investigated. The following are a few of the questions that might be studied:

Are there two hemolysins present — an autohemolysin and an iso-hemolysin?

If so, can they be separated? How do they differ?

Can both be entirely removed from the serum by absorption by red cells?

If so, will the remaining serum give a positive Wassermann reaction?

To what extent, if any, can the steps in the process be reversed?

What relation does this process of hemolysis bear to artificially induced hemolysis?

The chief points of clinical interest in this report are the sex of the patient, her present age of $3\frac{1}{4}$ years and the fact that the first attack occurred during the second year of life. This is I believe the youngest recorded case.

ADDENDUM

The infant brother referred to in the report died June 14, 1912. Necropsy revealed that the liver was very dark in color, moderately enlarged and somewhat friable. No spirochetes were found, and none of the internal organs showed definite evidences of syphilis.

137 Clinton Street.

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12. Kumagai and Jnoue: Deutsch. med. Wchnschr., 1912, No. 8, 361.
13. Charpentier: Hemoglobinuria. Balliere, Tindall & Co., London, 1910.
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15. Case here reported.

ON THE MODE OF INFECTION IN EPIDEMIC CEREBRO-SPINAL MENINGITIS *

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The *Diplococcus intracellularis* was identified as the specific excitant of epidemic cerebrospinal meningitis by Weichselbaum in 1887. The procedure of lumbar puncture as a means of obtaining cerebrospinal fluid and attaining an etiologic diagnosis in cases of meningitis was introduced by Quincke in 1891.

The studies of meningitis made possible by this means have established beyond question the relationship of the meningococcus to the epidemic type of meningitis which has presented itself in various parts of the world during the last decade. As this relationship has been made clear, the problem of the control of this dreaded disease has focused itself about the life of the specific organism, its distribution in the body of those affected by the disease, its paths of exit from the body, its viability, and the mode by which the infection might be conveyed to others. Most of the points of interest and importance in these relations have been quite thoroughly cleared up.

The meningococcus has been found not only in the cerebrospinal fluid of those suffering from the disease but in the conjunctiva and the eye, in the nose and throat, in the pleura and lungs, in the pus of joints, in the throat, and in the blood. So far as our present knowledge leads us, the organism may be excreted from the body by the purulent discharges from an active conjunctivitis or by the secretions of the nose, throat and bronchi. While the organism has been found in the conjunctival secretions by Koplik,¹ Robinson,² and others, and the possibility of contagion from that source must be recognized, active conjunctivitis is not a frequent accompaniment of the disease and infection from that source must be rare.

In like manner, as Jakobitz³ has shown, the meningococcus may be found in the lungs both in those suffering from cerebrospinal meningitis, with or without definite pulmonary complications, and in rare instances in pneumonias and bronchial catarrhs occurring independently of meningitis.

*Read at the meeting of the American Pediatric Society, Hot Springs, Va., May, 1912.

1. Koplik: Osler's Mod. Med., ii, 499.

2. Robinson: Am. Jour. Med. Sc., 1906, cxxxi, 603.

3. Jakobitz: Ztschr. f. Hyg. u. Infectious-krankh., 1907, lvi, 175.

The greatest interest and importance, however, attach to the presence of the meningococcus in the nose and throat, because its presence in these passages may not only be a ready means of disseminating the organism outside the body of the patient, but also suggests the possibility of direct infection of the meninges from this source.

Since von Lingelsheim directed attention to the fact that the organism was to be sought not in the nares but in the nasopharynx, the reports of its discovery in cases of meningitis have shown increasing positive results. With the question of the identification of the *Diplococcus intracellularis* we need not here concern ourselves. The work of Councilman, Mallory and Wright,⁴ Albrecht and Ghon,⁵ and von Bettencourt and Franca⁶ has made the differentiation of the meningococcus so certain that reports conforming to the established standards can be accepted as reliable.

From reports of the occasional finding of the specific organism in the nasal or nasopharyngeal secretions, we find more and more positive results recorded. Thus Goodwin and von Scholly⁷ obtained positive results from the nasal mucus of twenty-seven out of fifty-two (50 per cent., plus) cases examined during the first two weeks of the disease and Dieudonné four positive findings in six cases (67 per cent.) and von Lingelsheim⁸ under favorable conditions forty-six positive results in forty-nine examinations (93.8 per cent.). It seems probable that the organism is present in the nose or nasopharynx of most of the cases of epidemic meningitis during the early stages of the disease.

But it has also been found in the same site in well persons, especially in those who have been in contact with cases of meningitis and also in many in whom no knowledge of exposure can be obtained. Thus Goodwin and von Scholly found the specific organism in the nasal secretions of 10 per cent. of forty-five "contacts;" Dieudonné obtained five positive results in thirty-nine trials, and Fraser and Comrie¹⁰ ten in sixty-nine trials, of contacts.

In the effort to control the inroads of the disease in the German army, similar investigations have been made on a large scale in regiments exposed to the disease, with most interesting results. Hübener and Kutscher¹¹ report that in 400 men of one battalion they found eight

4. Councilman, Mallory and Wright: Epidemic Cerebrospinal Meningitis, Rep. Mass. St. Bd. Health, Boston, 1898.

5. Albrecht and Ghon: Wein. klin. Wchnschr., 1901, xiv, 984.

6. Von Bettencourt and Franca: Ztschr. f. Hyg. u. Infectious-krankh., 1904, xlv, 463.

7. Goodwin and von Scholly: Jour. Infect. Dis., 1906, p. 21.

8. Dieudonné: Centralbl. f. Bakteriöl., 1906, xli, Pt. 1, 418.

9. Von Lingelsheim: Klin. Jahrb., 1906, xv, 400.

10. Fraser and Comrie: Scottish Med. and Surg. Jour., 1907, xxi, 18.

11. Hübener and Kutscher: Deutsch. militär-arzt. Ztschr., 1907, xxxvi, 639.

coccus carriers although there were no cases of meningitis in the regiment itself at the time, and Vagedes¹² in 1,703 men examined under like conditions found ten carriers.

Under ordinary conditions the meningococcus quickly perishes outside the human body. It therefore seems highly probable that the spread of the disease depends on the presence of the specific organism in the nasal passages or respiratory tract of those sick with the disease and also of many persons in good health. The respiratory tract, and especially the nasopharynx, appears to be the usual portal of entry.

These facts being accepted, how does the organism from the nasopharynx or other part of the respiratory tract reach the meninges and there set up its specific inflammation?

The proximity of the nasopharynx to the meninges naturally suggested the possibility of direct infection. Of many contributions to the discussion of this subject, that of Westenhoeffer¹³ is based on the study of the most ample material and is of most interest.

As the results of his anatomic observations, Westenhoeffer lays emphasis on the following facts:

1. The meningitis begins at the base of the brain, in the region of the optic chiasm and about the hypophysis cerebri, and from this point spreads in all directions.
2. There is a suppurative exudate about the gasserian ganglion and in the sheaths of the several motor nerves of the eye.
3. Constant redness, swelling and hypersecretion of the nasopharyngeal tonsil and adjacent parts with an ascending otitis media.
4. The sphenoidal sinuses are constantly affected in all patients over 3 years of age. They were found markedly affected in twelve out of thirteen cases.
5. The antrum of Highmore is less often involved.
6. The ethmoidal sinuses are rarely and but slightly affected.
7. In all cases there is some swelling of the cervical lymph-nodes.

From these observations it seemed probable that there might be direct infection of the meninges from this nasopharyngeal focus through the sphenoidal sinuses. Especial emphasis is laid on the perihypophysial inflammation because of the close relation of the hypophysis to the sphenoidal sinuses and the known fact that in fetal life the sella turcica communicates with the throat through a hypophysial passage.

Two lymphatic paths are open for infection of the meninges from the nasopharyngeal process.

1. The infectious agent may make its way along the nerve sheaths, especially the several branches of the gasserian ganglion, as staphylococci,

12. Vagedes: *Deutsch. militär-arzt. Ztschr.*, 1907, xxxvi, 647.

13. Westenhoeffer: *Klin. Jahrb.*, 1906, xv, 657.

streptococci and typhoid bacilli have been shown by Homen to rise along the lymph channels of the sciatic nerve to the spinal cord. The inflammatory deposits surrounding these nerves are, however, readily shown to be secondary to the meningitis and descending, not ascending, processes.

2. The path of invasion may be along the carotid sheath to the region of the hypophysis.

However, investigation shows that the same perihypophysial inflammation is found in both otitic and tubercular meningitis. In the latter at least of these the infection undoubtedly reaches the meninges through the blood-stream and not by lymphatic channels. The value of the perihypophysial inflammation as evidence of the lymphatic transmission of the infection is therefore slight.

In the end Westenhoeffer admits the impossibility of proving the lymphatic transmission and assumes that the infection must reach the meninges through the blood-stream.

He even suggests that the whole throat affection may be secondary, although this seems improbable, inasmuch as it appears too early, in some cases before the onset of the meningitis, and also because the specific organisms are known to be often found in the throats of persons in good health (carriers).

Lymphatic transmission having apparently failed of proof, Westenhoeffer regards the infection as carried by the blood and probably by the arteries, inasmuch as no extensive thromboses are regularly present in cerebrospinal meningitis.

The cocci, as he says, are known frequently to be found in the blood, in some cases in the earliest stages of meningitis. In two or three cases lasting less than twenty-four hours, an endocarditis of the mitral valve and purulent myocarditis produced by the meningococci have been found.

Göppert¹⁴ similarly summarizes his study of this question in these words:

The whole respiratory tract, from the nose to the pulmonary alveoli, shows in the early stages of epidemic cerebrospinal meningitis more or less severe inflammatory changes. These may precede the onset. Chance brings one or the other—the pharyngitis, tonsillitis, pneumonia or bronchial catarrh, otitis media—of these conditions into the foreground. None of these affections is obligatory and therefore the opinion may be advanced that sometimes this, sometimes that point of the respiratory mucous membrane becomes the portal of entry of the meningococcus. Therewith must we accept the fact that the meningococcus may reach the brain through the blood channels, a conception which obtains support from the presence of the meningococcus in the blood.

Thus these two observers, disagreeing at the outset as to the importance of the local lesions of the respiratory tract, come in the end to agreement as to the probable route of infection of the meninges.

14. Göppert: *Klin. Jahrb.*, 1906, xv, 527.

At this point the problem of demonstrating a meningococcus septicemia, either as an attendant feature of epidemic cerebrospinal meningitis or independently of it, becomes of great interest.

That the meningococcus may be found in the blood in certain cases of epidemic meningitis has been known for some time. Gwyn¹⁵ first reported such a finding in a patient of Osler, and since then similar observations have been made by many others, Cochez and Lemaire,¹⁶ Jakobitz,¹⁷ Martini and Rohde,¹⁸ Lenhartz,¹⁹ Marcovitz,²⁰ Robinson²¹ and Duval.²² Elser,²³ in forty-one cases found the coccus in the blood in 10.25 per cent.; Dieudonné reports positive blood findings in four out of five cases, in one of which the nasal secretion was negative.

Especial interest, however, attaches to the presence of the meningococcus in the blood in patients free from meningitis. In 1908 I²⁴ reported the case of a girl of 15 years who presented some of the symptoms of cerebrospinal meningitis, but whose spinal fluid remained free from meningococci, while the organisms were found in the blood. At that time I was able to find in the literature three other reports of meningococcus septicemia without meningitis, these being recorded by Salomon,²⁵ Liebermeister²⁶ and Andrewes.²⁷ Netter has since recorded the case of a woman suffering from diarrhea, fever and general malaise, whose blood agglutinated two strains of meningococci, but whose blood culture was not taken. The patient's sister had cerebrospinal meningitis at the time.

Cecil and Soper²⁸ have collected from literature four cases of meningococcus endocarditis, two of these being the cases of Westenhoeffer already referred to, and add an observation of their own. The patients of Warfield and Walker²⁹ and Cecil and Soper gave no evidences of meningitis.

The occurrence of meningococcus septicemia both in conjunction with the cerebrospinal meningitis and independently of it, lends support to the view that the infection of the meninges is brought about through the blood, the primary focus being in the respiratory tract.

15. Gwyn: Bull. Johns Hopkins Hosp., 1899, x, 112.
16. Cochez and Lemaire: Baumgarten's Jahres., 1902, xviii, 91.
17. Jakobitz: München. med. Wehnschr., 1905, lii, 2178.
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22. Duval: Jour. Med. Research, 1908, xix, N. S. xiv, 258.
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26. Liebermeister: München. med. Wehnschr., 1908, iv, 1978.
27. Andrewes: Lancet, Lond., 1906, lxxxiv-ii, 1172.
28. Cecil and Soper: Arch. Int. Med., 1911, viii, 1.
29. Warfield and Walker: Bull. Ayer Clin. Lab., 1903-6, i-iii, 81.

Elser and Huntoon³⁰ summarize the evidence of hematogenous infection in these words:

The early appearance of the meningococcus in the blood in a considerable number of cases, the appearance of general sepsis suggested by some patients early in the disease, the lesions in parts far removed from the central nervous system found at autopsy of individuals who succumbed to the disease within twenty-four hours of its inception, and finally the appearance of characteristic lesions in the eye synchronously with manifestations referable to the central nervous system, all point to an early generalization of the meningococci, but are not competent to prove that such an infection antedated the meningeal involvement.

The experimental study of this problem has not yet yielded decisive results. Bettencourt and Franca⁶ failed to produce meningitis in monkeys either by rubbing cultures of the meningococcus into the nasal mucous membrane or by intravenous injection.

Flexner³¹ succeeded in producing meningitis in monkeys by intraspinal injection, the resulting meningitis having in this case also the basal distribution thought suggestive of nasopharyngeal infection.

Elser and Huntoon, by intravenous injections of *Streptococcus mucosus* in rabbits succeeded in producing a meningitis which in its onset and the distribution of lesions resembled the meningococcus meningitis of man.

Finally, we may say that the evidence at our command at present strongly suggests that the primary infection in epidemic cerebrospinal meningitis is respiratory, in most cases nasopharyngeal, and that the meningeal infection is developed through the blood.

Protection of the community therefore will demand not only the isolation of those sick with the epidemic disease, but the detection of the many unaffected "carriers." To what extent this may be practicable remains to be seen. In the restricted fields offered by regimental organizations, the German military officers have already applied these methods with apparent success.

The efforts to free carriers from their infection (nasopharyngeal) have, so far as I can learn, proved ineffective. Various applications, douches and insufflations have been tried without success. In this regard the experience seems to repeat that with diphtheritic infections of the throat. In time the infection appears to die out in most cases, but treatment does not hasten that desired end.

Our present knowledge would suggest the desirability of treating these persons by serum or vaccines. The possibility of protecting the exposed by like means naturally presents itself, but thus far I have not been able to learn of any work along these lines.

137 East Sixtieth Street.

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THE DIAGNOSIS OF ENLARGED BRONCHIAL GLANDS *

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The term bronchial glands, as usually applied, includes not only the lymph-nodes about the bronchi, but also the peritracheal, infratracheal and hilus groups. The tracheal group consists of from seven to ten nodes situated along either side of the lower part of the trachea, more numerous on the right and varying in size from a pea to the size of a bean. The bronchial glands proper include the infratracheal group and the glands about the stem bronchi. They attain their greatest size and are most numerous beneath the right bronchus. The tracheal glands are in relation to the superior vena cava and with the vagus and recurrent laryngeal nerves. The left recurrent nerve, because of its lower origin, is in contact with the trachea for a much longer distance and is more liable to compression than the right one. When these glands are swollen, they may be in contact with both common carotid arteries, innominate veins, arch of the aorta and the phrenic nerves. The group at the bifurcation of the trachea is posterior to the pericardium and anterior and slightly to the right of the esophagus. The vagus nerve is also in relation to this group. When enlarged, they may press on the spine to the right of the esophagus. The hilus glands are in contact with the bronchial and pulmonary vessels and with the lung. As the trachea extends downward it inclines to the right so that at its lower end it is in the right sternal line anteriorly, and to the right of the center of the vertebral column posteriorly. The point of bifurcation in children is about the fourth thoracic vertebra and in adults at about the intervertebral cartilage between the fourth and fifth thoracic. From the arrangement of the lymph-nodes in Figures 1 and 2 it is seen that they are considerably more numerous on the right than on the left. Enlargement of the bronchial nodes may be present in any disease affecting the lymphatic nodes throughout the body, as, for instance, Hodgkins' disease or lymphatic leukemia, with malignant dis-

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eases of the lung and with various pulmonary infections. In a patient convalescent from scarlet fever who developed enlarged cervical glands, I was able to detect a synchronous enlargement of the bronchial nodes. A very large percentage of these enlargements, however, are of a tuberculous nature. It has long been known that a tuberculous infection of the nodes may antedate the involvement of the lung by months or even years, yet until comparatively recently but little attempt has been made to diagnose the condition while it is still limited to the bronchial nodes. According to Harbitz,¹ the bronchial nodes, using the term in its strict sense, are not as often the source of the primary infection as those of the hilus.

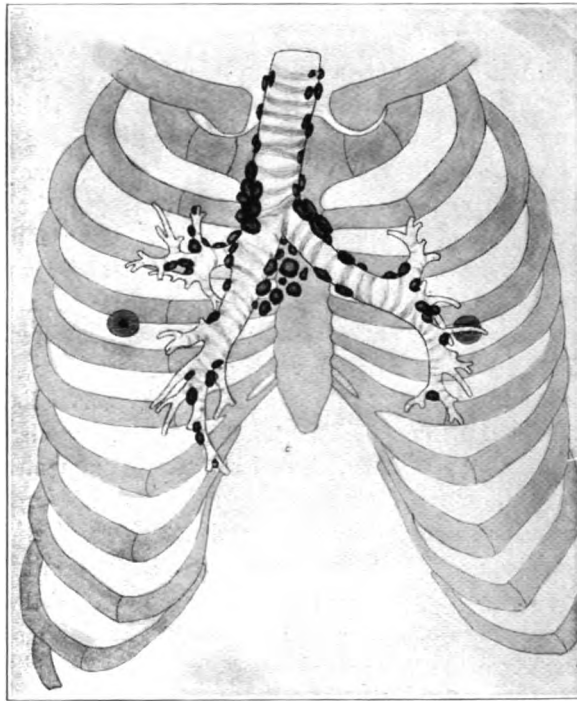


Fig. 1.—The relationship of the bronchial glands to the anterior thoracic walls of the adult. In the child the bifurcation of the trachea is behind the right of the sternum at the level of the third costal cartilage. The glands are according to Sukiennikow (*Berl. klin. Wehnschr.*, 1903, xl, 316, 347, 369), and the trachea and bronchi are after Blake (*Am. Jour. Med. Sc.*, 1899, cxvii, 320).

tracheal or infratracheal groups. Wollstein² found the largest nodes on the right side in 74 per cent. of her cases. Infection of the lung takes place either as the result of rupture of a caseous node into a bronchus or

1. Harbitz: *Jour. Infect. Dis.*, 1905, ii, 143.

2. Wollstein: *Arch. Int. Med.*, 1909, iii, 221.

by way of the lymphatics. In children under 1 year, Sluka³ always found, by means of the *x*-ray, that the disease had extended beyond the nodes unto the lung.

SYMPTOMS

In a great many instances slight involvement of the bronchial lymph-nodes causes no symptoms. While the children with tuberculosis of these nodes are usually delicate in appearance, such is not always the case. Both adults and children may look the picture of health, even when the symptoms and signs are definite. The realization of this is of the utmost importance. When tuberculous, the symptoms are in part caused by the toxin of that disease and in part are the result of pressure. We find that

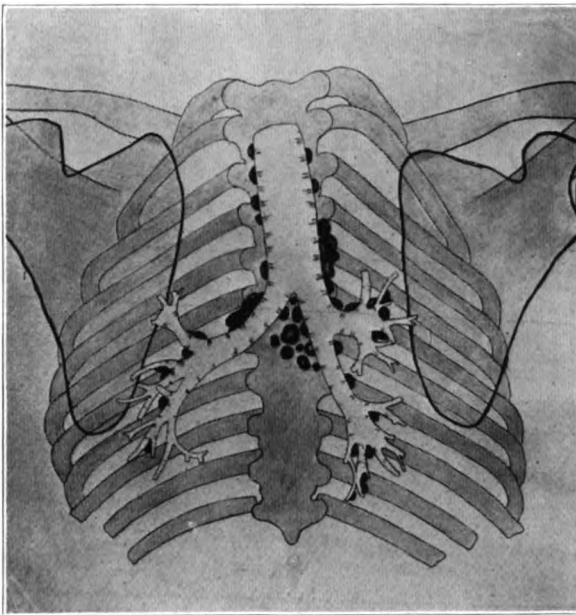


Fig. 2.—The bronchial glands as seen from behind. In the child the trachea bifurcates at about the level of the intervertebral disk between the fourth and fifth thoracic vertebræ which corresponds nearly to the tip of the fourth thoracic spine (Blake). It is slightly lower in the adult. This drawing and the preceding one are from radiographs of an adult cadaver into whose trachea a metallic alloy had been injected.

these patients are easily fatigued, capricious in appetite and often irritable in disposition. The insidiousness of onset and the lack of definiteness of the symptoms is quite characteristic. An interscapular backache is sometimes complained of and, when present, it will usually be found that pressure over the upper thoracic spines will elicit tenderness. Sometimes

3. Sluka: *Wien. klin. Wchnschr.*, 1910, xxiii, 156.

a more or less constant pain is complained of within the thorax. It rarely can be definitely located, but is usually between the mammary lines. Sometimes it is sharp and darting in character and it may be brought on by deep breathing or extra exertion. Vasomotor instability is shown by the flushing of one or both cheeks; this is sometimes a very annoying symptom. Puffiness of the face and especially under the eyes from pressure on the venous trunks may give the facies of nephritis. The superficial thoracic veins are often dilated. Increased frequency of the pulse is often present and the temperature is apt to be low in the morning and may reach 99 F. or higher in the afternoon, though it may be sub-

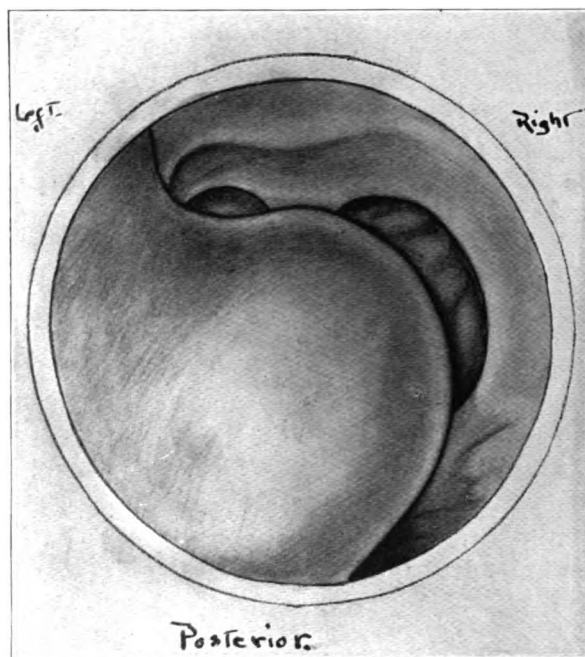


Fig. 3.—Bronchoscopic appearance in a case of tracheal compression from enlarged bronchial glands (Guisez). The extreme dyspnea was at once relieved by the bronchoscope, which was introduced very easily.

normal continuously. Krämer⁴ has observed an increased sensitiveness to cold, especially in the region of the shoulders. There may be more or less indigestion, hydrochlorhydria, according to Philippi,⁵ being most frequently present. In women all of these symptoms are apt to be more marked at the menstrual period. A brassy cough is usually the first thing to excite concern, although the glands may reach a large size with

4. Krämer: Beitr. z. klin. d. Tuberk., 1909, xiv, 335.

5. Philippi: Beitr. z. klin. d. Tuberk., 1911, xxi, 67.

practically no cough, as they did in the case from which Photographs 10 and 11 were taken. The paroxysms of coughing may be so severe as to resemble whooping-cough, frequently gagging results and sometimes even vomiting. In some instances patients have to support themselves by holding on to something during these coughing spells. The caseous node may be expectorated after rupture into a bronchus, as occurred in Hall's⁶ case.

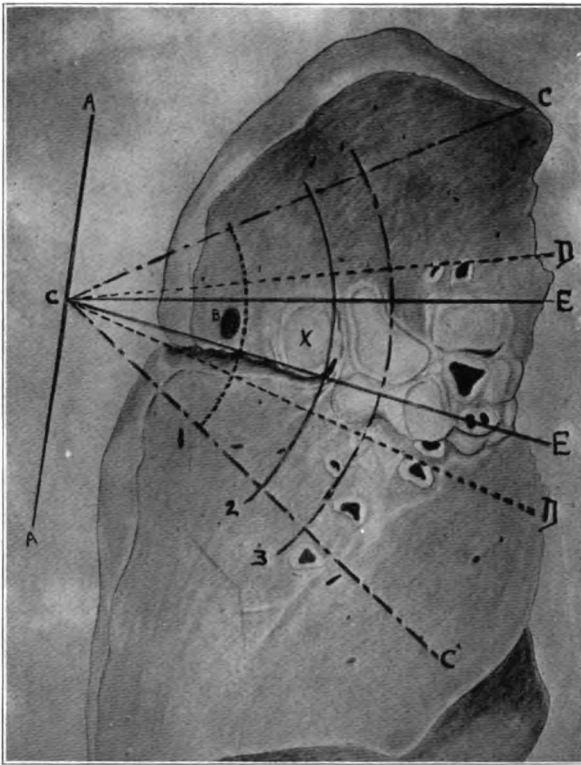


Fig. 4.—Antero-posterior section of a lung showing bronchial glands (Northrup). The line A represents the skin surface in the interscapular space; B, area of consolidation. The triangle C-C-C shows the vibrating area with heavy percussion; D-C-D, light percussion; E-C-E, very light or tapping percussion. Arc of circle No. 1 shows sufficient penetration for a superficial lesion B, but insufficient to reach gland X; Arc 2 represents the essential depth, attained with both light and very light percussion; Arc 3 shows that the slightly increased depth obtained with heavy percussion is not in proportion to the increased width of the vibrating area.

In infants dyspnea may be the most marked symptom. As a rule, it is chiefly or wholly expiratory in character and due seemingly to a vagus

6. Hall: *Am. Jour. Med. Sc.*, 1899, cxviii, 185.

neuritis from the pressure of the swollen nodes. This was so in Hoover's⁷ case, and Viro and Guinon⁸ also found that the stridor was caused by nerve irritation rather than direct compression of either trachea or bronchus. Einthoven,⁹ moreover, was able to throw the bronchial muscles into spasm by vagus stimulation.

Schick,¹⁰ however, thinks compression of the trachea and bronchi occurs more often than is usually stated, and Guisez¹¹ reports a case

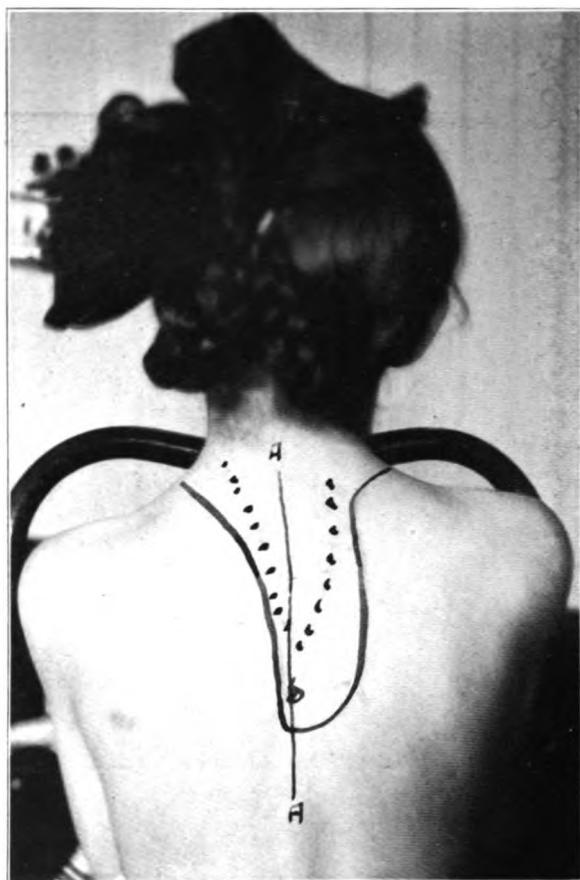


Fig. 5.—A A, line of vertebral spines. Continuous line includes area of bronchial gland dulness. Dotted line shows area over which whispered bronchophony was heard. For x-ray picture, see Figure 16.

7. Hoover: Jour. Am. Med. Assn., 1911, lvii, 1734.

8. Viro and Guinon: Quoted by Aviragnet, Bull. Soc. de pédiat. de Paris, 1911, No. 3, 126.

9. Einthoven: Quoted by Hoover (see note 7).

10. Schick: Wien. klin. Wehnschr., 1910, xxiii, 153.

11. Guisez: Bull. Soc. de pédiat. de Paris, 1911, No. 3, 144.

from which Figure 3 is taken, and in which there was marked tracheal compression. It would seem that compression might easily occur when the pressure was exerted from behind, owing to the absence of cartilage posteriorly.

The dyspnea of infants is divided into three classes by Marfan,¹² first, wholly inspiratory, due either to congenital vestibulo-laryngeal stenosis or paralysis of the dilators of the glottis; second, expiratory and inspiratory, but chiefly the latter, usually caused by the pressure of an enlarged

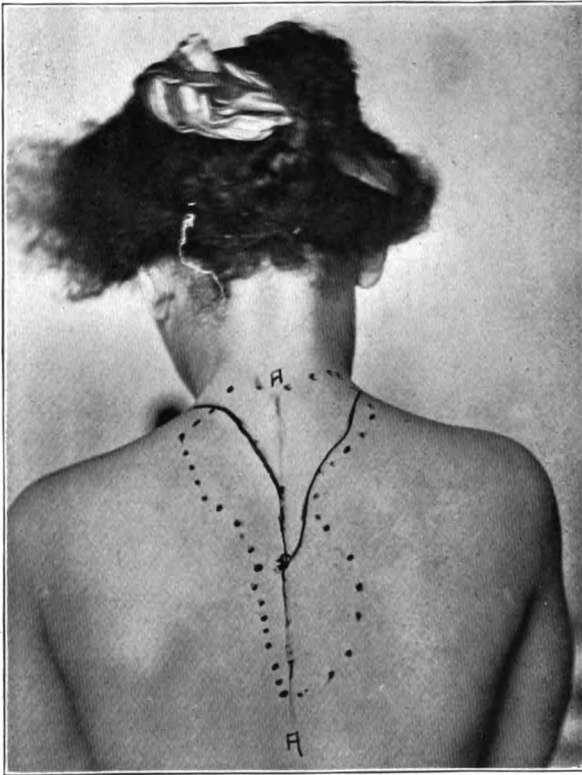


Fig. 6.—The outward dislocation of the upper inner line of pulmonary resonance is here shown, more marked on the right than on the left. The dotted lines show wide area of transmission of the whispered voice. For *x*-ray picture, see Figure 17.

thymus; third, chiefly or exclusively expiratory, the result of stenosis from either tracheal or bronchial nodes.

Aviragnet¹³ has reported a case in which the stridor was wholly inspiratory and for this reason an enlarged thymus was diagnosed. At

12. Marfan: *Bull. Soc. de pédiat. de Paris*, 1911, No. 3, 131.

13. Aviragnet: *Bull. de la Soc. de pédiat. de Paris*, 1911, No. 3, 126.

the autopsy a large number of tuberculous lymph-nodes were found, in which were imbedded the recurrent laryngeal nerves. The dyspnea in this case was presumably due to paralysis of the dilators of the glottis. Dyspnea developing after an acute pulmonary infection is usually due to swollen lymph-nodes rather than to an enlarged thymus. Schick¹⁰ observed that the expiratory stridor was more apt to be present when the child was resting quietly and that a hard attack of coughing or the disturbing of the infant would cause the dyspnea temporarily to disappear.

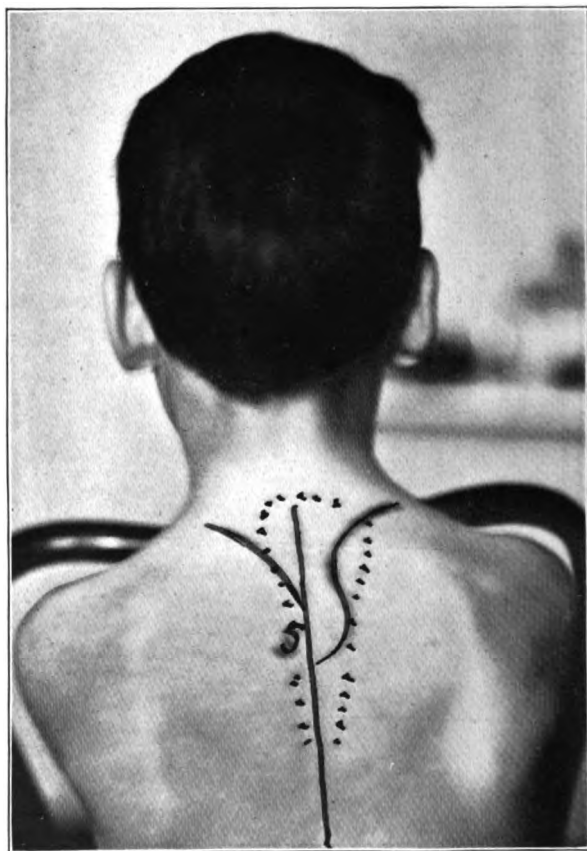


Fig. 7.—As in the two preceding pictures the dulness is indicated by the continuous line, the bronchophony by the dotted one.

He has known intubation to have been performed under the belief that the case was one of laryngeal diphtheria. This mistake will not occur if it is recalled that in the latter condition the voice is lost, but present with enlarged glands. D'Oelsnitz¹⁴ has found that with urgent dyspnea from

14. D'Oelsnitz: Bull. Soc. de pédiat. de Paris, 1911, No. 6, 304.

an enlarged thymus the inspiratory retraction below the diaphragm and above the sternum and clavicle is about equal, but that when enlarged tracheo-bronchial nodes are the etiologic factor, the subdiaphragmatic retraction greatly exceeds that at the superior thoracic aperture. The simultaneous retraction in the epigastrium, the lower sternal region and in both hypochondria seeming to make the upper part of the chest bulge forward with inspiration.

Dyspnea in adults without adequate pulmonary, cardiac or renal lesion should make one think of enlarged mediastinal glands as a possible cause.

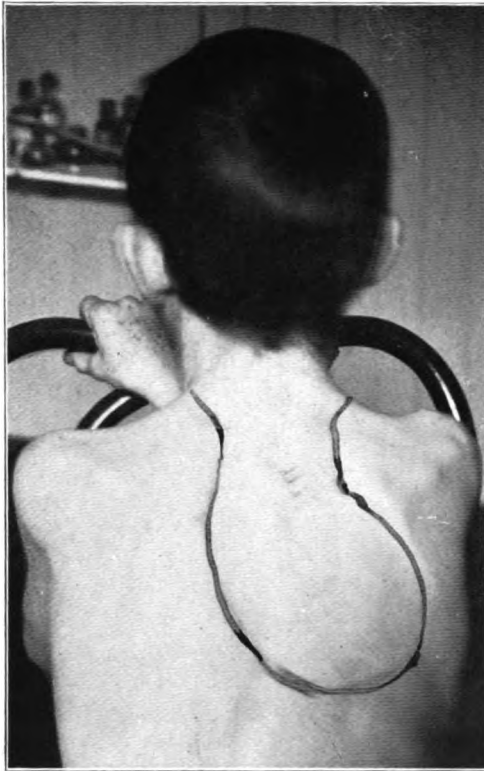


Fig. 8.—Marked interscapular dulness in a patient with mitral stenosis and regurgitation and secondary tricuspid insufficiency. No whispered bronchophony.

In a patient of Hoover's,⁷ with aortic aneurism in whom attacks of dyspnea were extreme, a marked degree of neuritis of the vagus was found at autopsy. Figures 10 and 11 show how far the nerve may be displaced from its normal position by the swollen nodes.

Hemorrhages may take place as the result of erosion of a blood-vessel from pressure, and fatalities have occurred in some instances. More common is the expectoration of smaller amounts of blood. The way in

which this is brought about was described so admirably by Coley¹⁵ in an excellent article over sixty-five years ago on bronchial-node tuberculosis that I will quote him verbatim:

When the return of blood from the head is obstructed by a considerable enlargement of the bronchial glands, and innutrition and enervation have been rapidly advancing, a sudden impulse given to the circulation by passion or otherwise may occasion a copious extravasation of blood from the venous capillaries into the pulmonary or bronchial mucous membrane which may leave behind it no other lesion than an appearance of ecchymosis.

In substantiation of which he cited a case reported by Barthez and Rilliet,¹⁶ in which there was congestion at the tracheo-bronchial junction. Griffin¹⁷ likewise reported intense hyperemia of the trachea at its bifurcation, associated with enlarged and caseous nodes, in a man of 28, who died with the symptoms of hemorrhage. I have had under observation a boy who has expectorated blood several times, and both physical examination and the x-ray show enlargement of the bronchial nodes, but no pul-

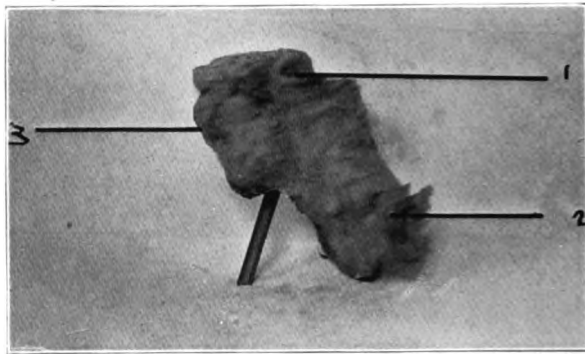


Fig. 9.—1, Trachea. 2, Left bronchus. 3, Glands along trachea above right bronchus. Whispered voice present over upper four thoracic spines.

monary involvement. Dr. Lewis G. Cole tells me he has made radiographs of several similar cases. It is my belief that signs of bronchial-node enlargement will usually be found in the patients who have hemorrhages without evidence of pulmonary or cardiac lesion. Paralysis of the vocal cords (usually the left) is suggested by a hoarseness of the voice, while the unilateral dilatation of the pupil—an uncommon sign—points to pressure on the sympathetic. Sometimes one can observe a delayed expansion of one side, even without pulmonary involvement. Palpation, though greatly inferior to percussion and auscultation, is sometimes of

15. Coley: *A Practical Treatise on the Diseases of Children*, 1846, p. 185.

16. Barthez and Rilliet: *Traite de malad. des enfans.*, iii, 172, quoted by Coley (Note 15).

17. Griffin: *Med Rec.*, New York, 1891, xxxix, 166.

considerable value. Tenderness to pressure over the mid-thoracic spines to which Petrushky¹⁸ called attention some years ago, is present in children and also in adults when the toxic symptoms of tuberculosis are marked, but it is not found in the latent cases nor in those in the

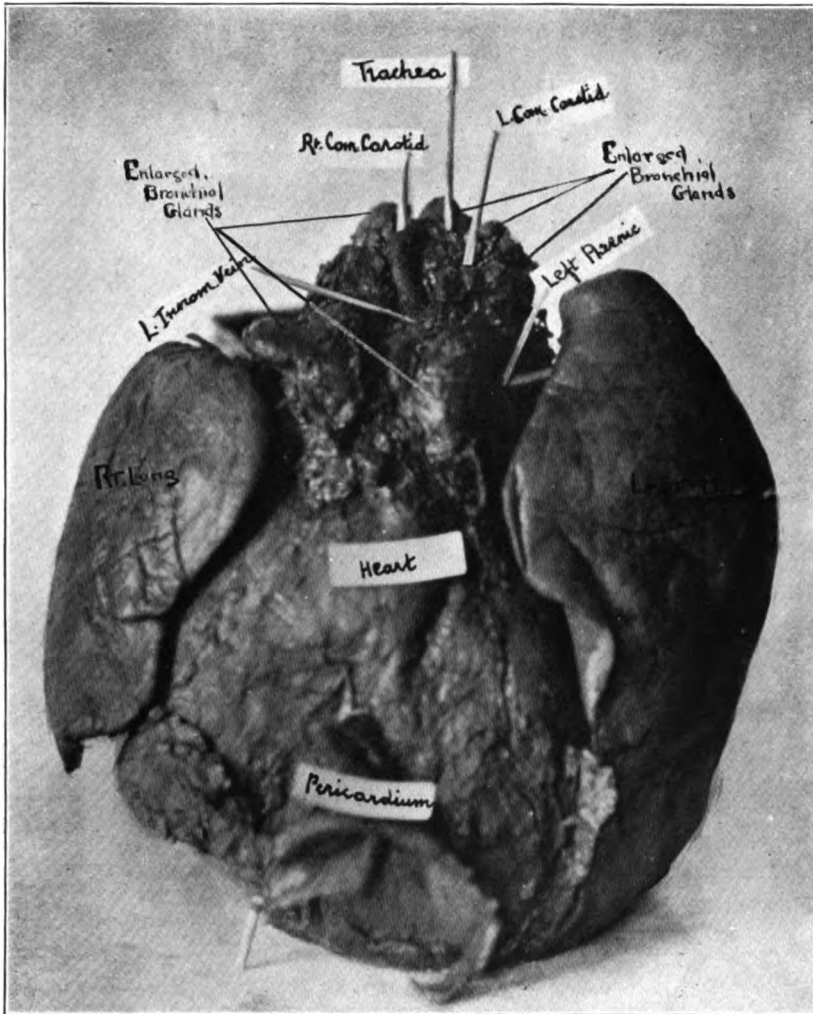


Fig. 10.—Anterior view of the mediastinal contents from a case whose only constant physical sign during life was whispered bronchophony in the interscapular space. Upper part of right lung has been resected.

advanced stages, and both rest and tuberculin treatment cause its prompt disappearance. Spinal tenderness of neurasthenia is not limited to the

18. Petrushky: München. med. Wchnschr., 1903, i. 364.

upper thoracic vertebra. De la Camp¹⁹ found spinalgia in 87 per cent. of 100 incipient cases. He states that the pain is present with recent inflammation, but not with cheesy nodes. Unless the tenderness is definite it is not of significance. The change of facial expression and the approximation of the scapula when the tender spines are palpated, are the most significant evidence. Tenderness to deep palpation along the sides of the neck just below the larynx is probably an indication of vagus hypersensitiveness induced by the pressure of enlarged nodes. Dautwitz²⁰

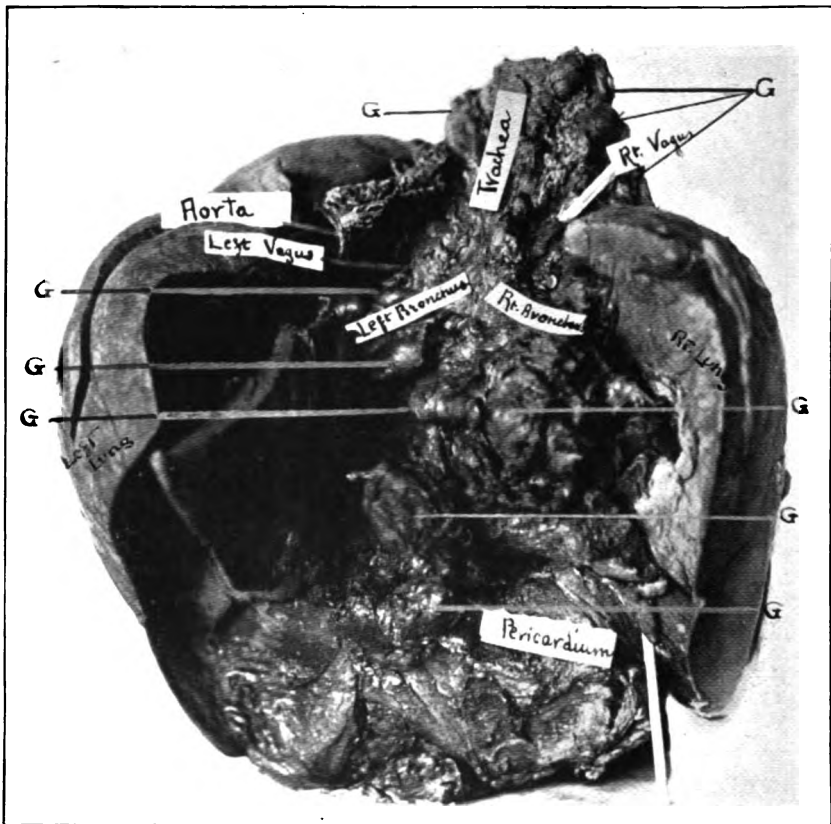


Fig. 11.—Posterior view of the thoracic viscera of patients referred to in text of Figure 10. Glands indicated by G. A large part of both lungs have been removed.

lays particular stress on the tenderness elicited by pressure over the sternoclavicular junction. The pain so occasioned may extend to the shoulder.

19. De la Camp: Quoted by Nagel. *Jahrb. f. Kinderh.*, 1908, lxxviii. 46.

20. Dautwitz, *Beiheft z. med. Klin.*, 1908. iv, No. 9.

PERCUSSION

The bronchial lymph-nodes lie so deeply that on first consideration it would seem quite unlikely that enlargement thereof could be detected by means of percussion. That this is often possible I am confident, providing, however, that a definite plan be followed in the examination and

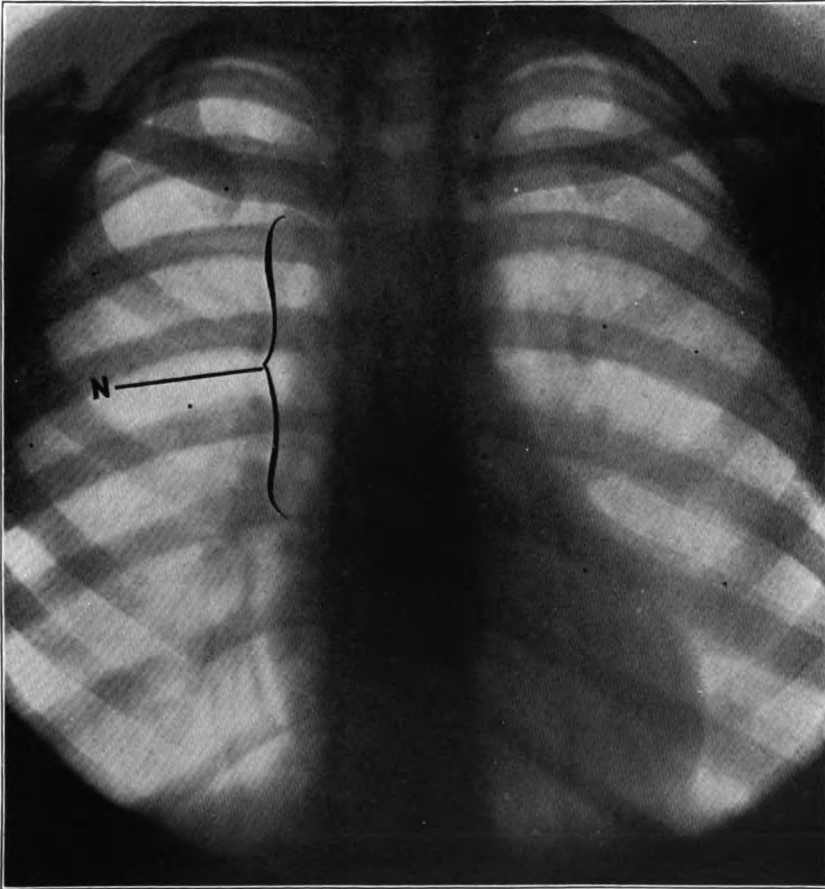


Fig. 12.—W. E. (216). This patient presented no signs of bronchial gland enlargement, and was twice negative to the skin tuberculin test. Lungs well aerated, except at both apices, where a suggestion of mottling is to be seen. A few calcareous hilus glands seen to the right of the heart. One should observe the normal contour of the right border of the heart (N). The subsequent pictures of patients with bronchial glands show a distinct bulging from the third space upward on the right of the vertebral column.

the percussion be sufficiently delicate. Notwithstanding that practically all articles dealing with physical diagnosis state that light percussion is more valuable than heavy, the majority of physicians percuss too hard.

If we digress for a moment to consider briefly the physics of percussion, the advantage of the light method will be apparent. When a blow is struck on the surface of an object, the area caused to vibrate is within a cone whose apex is at the point struck. The energy of percussion tends to be propagated in a line perpendicular to the surface and the diameter of the cone at its base bears a direct relation to the force of the blow. Let us apply these principles to Figure 4 (from Northrup), of an antero-posterior section of the lung, showing marked enlargement of the bron-

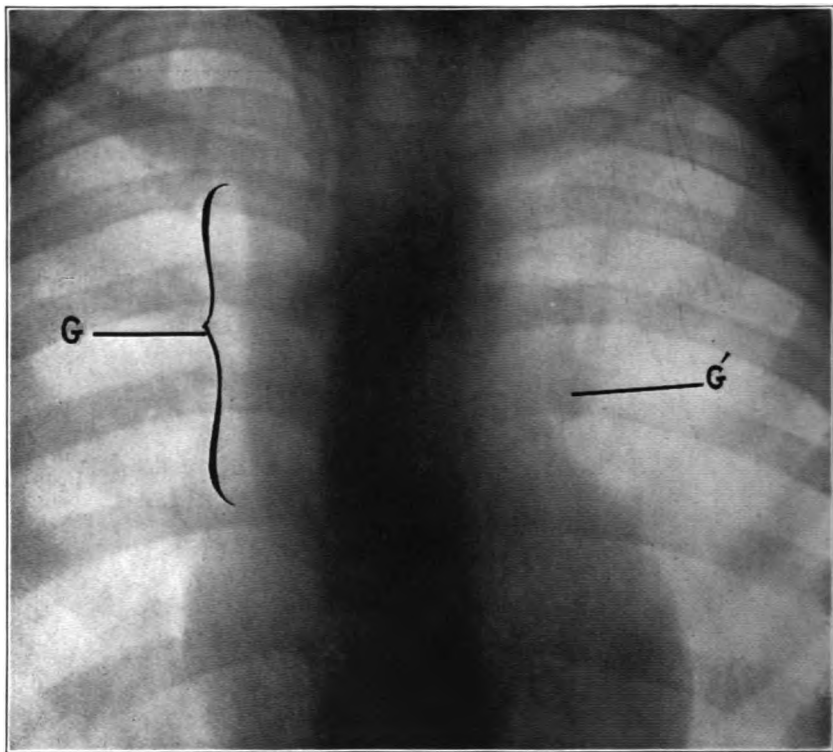


Fig. 13.—A. H. (209), aged 11. Retraction above right clavicle, and diminished expansion at right apex. Dilated veins over the front of the chest. Tender over fifth thoracic vertebra, less so over the upper four thoracic spines. Dulness to the fifth thoracic vertebra. Vertebral bronchophony, negative when first examined but later well marked. Tuberculin test negative. X-ray diagnosis: Normal markings of lungs show distinctly. Heart normal in size and position. Deficient aeration of and mottling of right apex. Enlarged bronchial glands, extending from the first to the third rib on the right (G), and on the left, opposite the cartilage of the second rib (G').

chial nodes. The line *A-A* represents the skin surface. In the triangle with dotted lines (*D, C, D*), which represents light percussion, all the sound waves are obstructed by the bronchial nodes and a dull note is

obtained. Heavy percussion is indicated by the triangle with the dot and dash line (*C, C, C*) and the dulness will be imperceptible, as so many of the sound waves pass by into the resonant lung. The futility of employing strong percussion for deep-lying lesions is thus apparent. While the triangle with dotted lines (*D, C, D*) depicts satisfactory percussion for the large lymph-nodes here shown, it would be too hard if only node *X* were present. On the other hand, much light percussion, shown by the triangle with the continuous line (*E, C, E*), would reveal

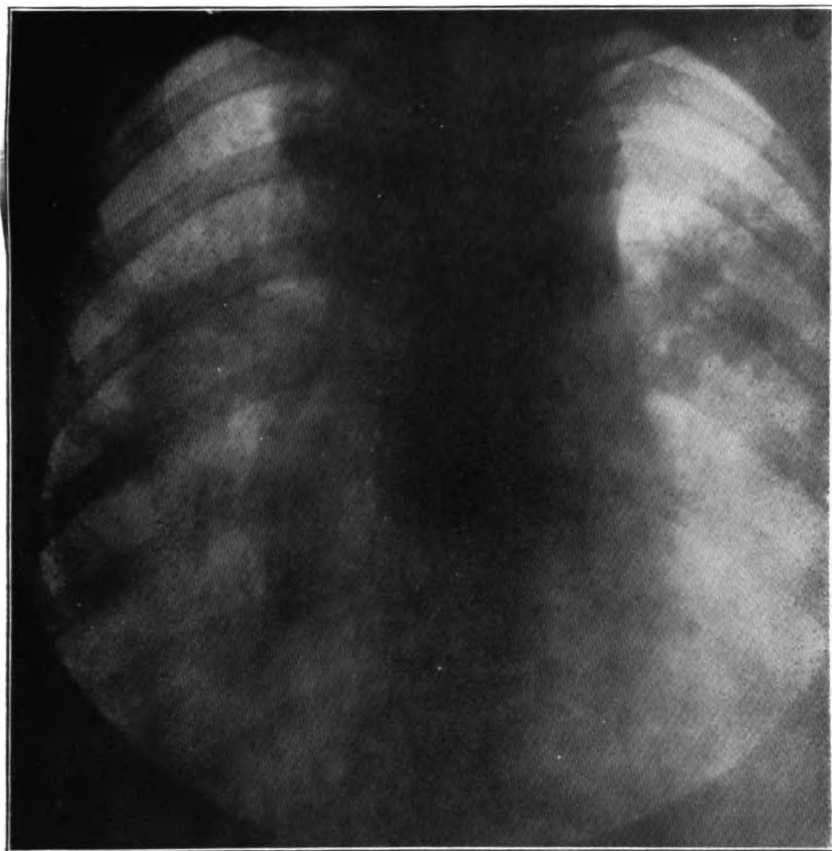


Fig. 14.—Hodgkins' disease. Edema of chest wall, arms neck and face. Marked substernal dulness. Paravertebral dulness slight. Whispered bronchophony marked over sternum and to a less extent in interscapular space. Normal markings of mediastinum obliterated by the huge mass of glands. Note "mushy" appearance.

this, and be equally as satisfactory when the nodes were of the size here shown.

In order that the percussorial energy may reach the deep-lying object, a certain force is necessary, and the arc of a circle with a continuous line

(2), represents the essential penetration. While the depth is somewhat increased with the force of the blow—arc with broken line (3)—it does not increase in proportion to the width, as the triangle with the dotted line (*C, C, C*) shows. Arc 1, depicts percussion too light to reveal node *X*, but sufficiently strong for a lesion at point *B*. In order to determine how forcible a blow is required in a given case, Turban²¹ suggests percuss-



Fig. 15.—Male patient, aged 49, with signs of very early infiltration at right apex. Vertebral and paravertebral dulness and increased whisper were present in the interscapular space. The radiogram shows great increase in size of central shadow, the normal markings of which are obliterated. Transverse diameter of the root of the lungs markedly increased, and in the *x*-ray plate a deficient aeration of the right apex is shown. Twice negative to the von Pirquet tuberculin test, he subsequently reacted positively to the subcutaneous test. Owing to a general lymphatic enlargement it is quite likely that he had Hodgkins' disease. The mediastinal shadow resembles the one in Figure 14.

21. Turban: *The Diagnosis of Tuberculosis of the Lungs*, New York, 1906, p. 69.

ing thrice on the same spot, first lightly, then slightly more forcibly and finally employing Ebstein's²² "touch percussion," which is merely a tapping with the middle finger of the right hand without wrist motion on the terminal phalanx of one of the fingers of the left hand, the little finger being the one of choice, as it causes the smallest amount of surface vibration. Turban has frequently demonstrated at autopsy nodules indicated during life by Ebstein's percussion when other methods were



Fig. 10.—Radiograph of child shown in Figure 5. B indicates cross section of a bronchus and small glands are shown at G.

doubtful. I thoroughly agree with Turban that this tapping percussion is greatly to be preferred in children and in adults with poor muscular development and with but little subcutaneous fat. It is not applicable,

22. Ebstein: Berl. klin. Wehnschr., 1894, Nos. 26 and 27. Quoted by Turban (Note 21).

on the other hand, in the obese, or in the presence of great muscular development. The following method of eliciting bronchial node dulness has been found satisfactory:

The patient seated on a stool in front of the examiner, who is also seated, crosses his arms over his chest, the fingers passing to the posterior axillary fold of the opposite side. To secure relaxation of the spinal muscles, which when contracted, give a dull note, the cervical and upper

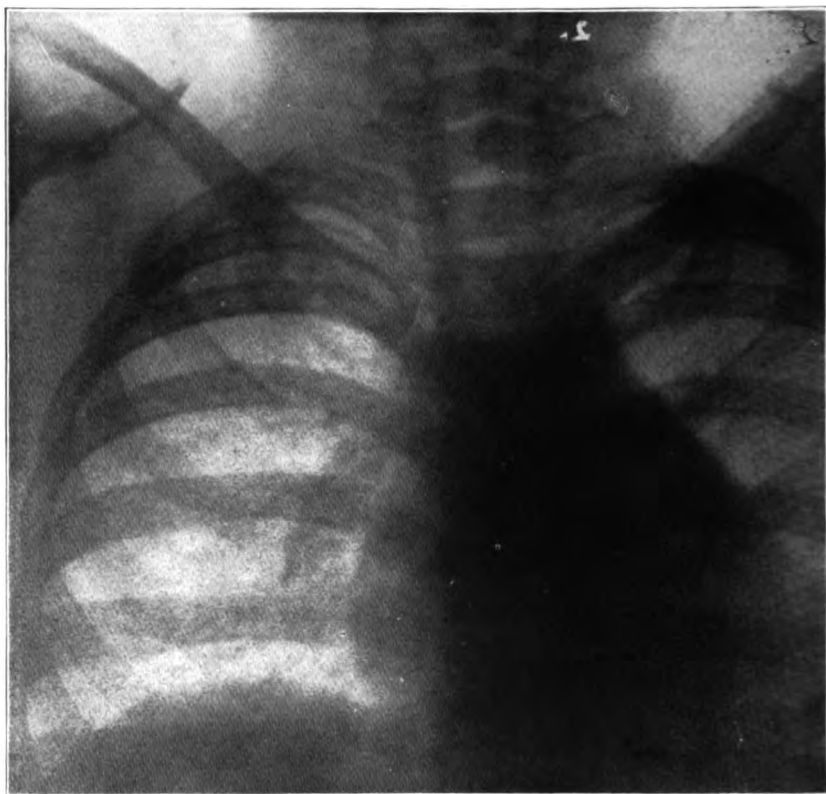


Fig. 17.—The mottled appearance along the descending branch of the right bronchus (seen to the right of the heart) probably due to the tuberculous peribronchial infiltration. The physical signs in this patient are shown in Figure 6.

thoracic vertebra are slightly flexed. Too great flexing must be guarded against, as it diminishes somewhat the area of bronchial gland dulness, though just why is not clear. The upper inner border of the lung as outlined by König's method, curves up to the side of the vertebral column at a point opposite the inter-articular cartilage between the second and third thoracic spines, but with enlargement of the tracheal

glands this normal curve is displaced outward and may not reach the vertebra until the fourth or fifth dorsal (Figs. 5, 6 and 7). When dulness extends outward from the fifth or sixth thoracic vertebra, it is probable that the bronchial and hilus nodes are enlarged. Bing²³ believes he is able to detect a normal dulness at the root of the lung opposite the fifth thoracic spine, the area being slightly larger on the right than on

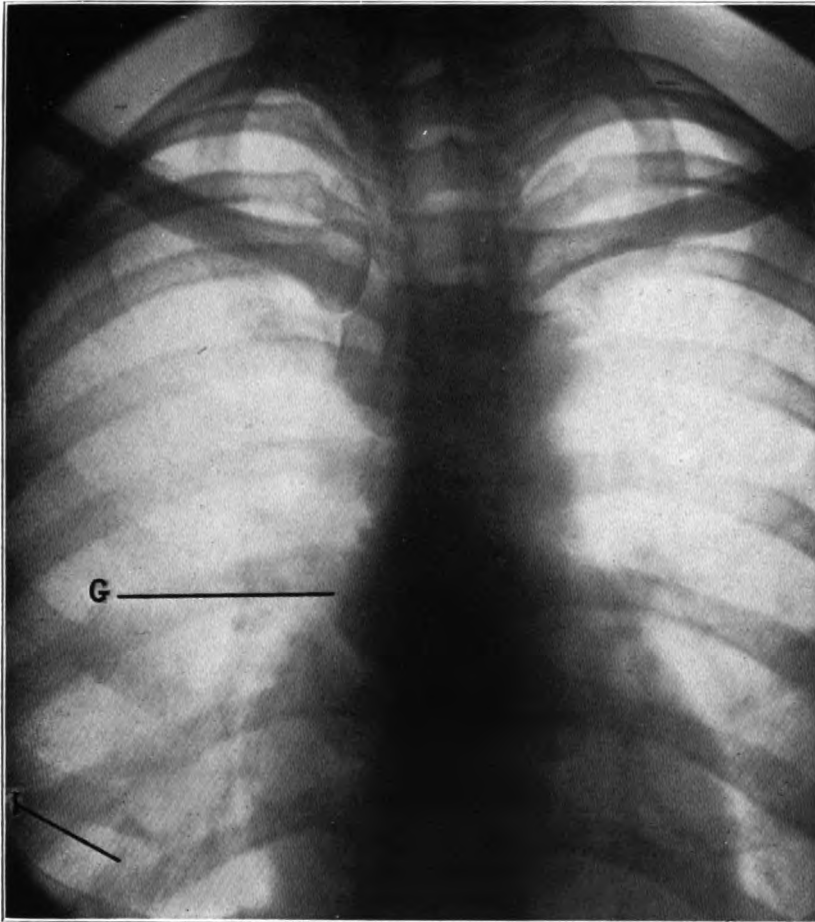


Fig. 18.—Adult woman. Infratracheal gland is shown at G. The bulging from peritracheal nodes is not present. At I is a small area of infiltration. The chief physical signs were exquisite vertebral tenderness over the upper thoracic vertebra, slight dulness in the second interspace to the right of the sternum, vertebral dulness to the fifth thoracic vertebra and paravertebral dulness opposite the fourth or fifth thoracic. Vertebral bronchophony was present but not well marked.

23. Bing: *Ugesk. f. Læger*, 1910, lxxii, 199. Also *Berl. klin. Wehnschr.*, 1910, xlvii, 376.

the left. I have been unable to confirm this. Not only should the resonance of the two sides be compared, but one should percuss each side from above downward, from below upward, from within outward and without inward. The outer border of dulness is the most difficult to determine. A blue pencil should be employed, and verifying one's markings with the eyes closed is an excellent way to determine one's percussorial ability. As Figures 1 and 2 show, the nodes are more numer-



Fig. 19.—Adult woman. Paravertebral and vertebral dulness to the sixth thoracic vertebra. Whispered bronchophony very marked and heard over the whole of the posterior aspect of the thorax. Note increased width at the root of the lungs, to the right of the vertebral column in first and second interspaces. Considerable increase in the right hilus shadow is seen in the third interspace. The right oblique position showed post-cardiac glands.

ous to the right, and for this reason the dulness is often limited to the right, and when bilateral, is usually more marked on that side.

In an endeavor to determine how large a node must be to be detected percussorially, Krämer⁴ injected wax into a cadaver just anterior to the vertebra, and found that when it was in the trachea or beneath the pleura

he could obtain dulness with 15 c.c., but not with 10 c.c. It seems quite probable that the bronchial glands are not alone responsible for the dulness. Nagel¹⁹ believes that there is an actual lessening of the amount of lung tissue as the result of the displacement caused from the glands. Krämer⁴ is of the opinion that the engorgement of both the lymph and blood-vessels as the result of obstruction at the hilus is responsible for a considerable amount of the dulness, and he draws attention to the fact that the x-ray does not show as large glands as might be expected from the extent of the dulness. Phillippi,⁵ on the other hand, thinks that the stasis in the lymph and blood-vessels plays an insignificant part, and he considers an inflammatory condition of all the hilus structures as the chief factor. That this is probably near the truth, the operative observation of Veau²⁴ shows. He operated on a patient with urgent dyspnea with a view of performing a thymectomy, but found only enlarged tracheo-bronchial nodes and a general mediastinitis. It is quite probable that all the above-mentioned factors contribute more or less to the dulness.

With slight apical involvement an area of normal resonance may be present between the dulness from the pulmonary lesion and that of the bronchial nodes. Von Koryni,²⁵ Ewart,²⁶ De la Camp²⁷ and De Costa²⁸ consider vertebral percussion superior to paravertebral. In adults a dull note is present normally over the first four dorsal spines. Ewart states that the fifth spine is normally dull, but this I think questionable. A distinctly dull note below the fourth spine is abnormal and may be indicative of mediastinal glands. In young children a resonant note is obtained over the fourth thoracic and not infrequently over the third. Because of the diminutive size of the spinous processes in the very young and their close proximity vertebral percussion is more difficult to perform than paravertebral. The absence of vertebral dulness has little weight in excluding bronchial node enlargement as it occurs much less frequently than paravertebral dulness. It is more apt to be present when the paravertebral dulness is bilateral.

Three children with mitral regurgitation and one with mitral stenosis and regurgitation with secondary tricuspid insufficiency had dulness in the interscapular space. It would seem that the dulness in these cases was due to dilatation of the left auricle, which the frozen sections of Fetterolf and Gittings²⁹ show is the most posterior chamber of the heart.

24. Veau: Bull. Soc. de pédiat. de Paris, 1911, No. 2, 83.

25. Von Koryni: Handb. d. spec. Path. u. Therap., 1897, iv, 717. Quoted by De la Camp (Note 19).

26. Ewart: Lancet, London, 1899, ii, 261.

27. De la Camp: Ergeb. d. inn. Med. u. Kinderh., 1908, 556.

28. De Costa: Am. Jour. Med. Sc., 1909, cxxxviii, 815.

29. Fetterolf and Gittings: AM. JOUR. DIS. CHILD., 1911, i, 6.

The right auricle undoubtedly contributed to the dulness in the case of tricuspid insufficiency. The extent of the dulness varied at different examinations, which is quite consistent with what we know concerning the dilatation of the auricle. In these cases it was at a somewhat lower level than the dulness from bronchial nodes (Fig. 8).

It is much less common to obtain dulness from the bronchial nodes anteriorly. When the nodes about the right bronchus are of considerable size, it is sometimes obtained in the second right space near the sternum. If the tracheal glands are much swollen, a dull note may be detected in the first space, just to the right of the sternum and possibly over the right half of the manubrium sterni. The slight dulness often present in the first right interspace near the sternum is due, according to Fetterolf and Norris,³⁰ to the more anterior position of the large vessels of the right side and to a relatively smaller amount of pulmonary tissue. Sternal dulness in children is nearly always due to an enlarged thymus, which may persist, Dautwitz states,²⁰ to the twelfth or thirteenth year. This thymic dulness usually extends to the left in the first interspace for a centimeter or more. Boggs³¹ has drawn attention to the fact that the lower border of thymic dulness moves upward when the head is markedly extended. Whether this occurs with bronchial nodes, I do not know. The possibility of an enlargement of the thyroid wholly intrathoracic in character should be considered with substernal dulness in adults. Proof that this may occur comes from the Mayo Clinic. The symptoms of hyperthyroidism and early tuberculosis, moreover, have much in common. It is frequently stated that in early lesions, with right apical diseases, there may be an increase of cardiac dulness to the right as a result of the lateral displacement of the anterior border of the right lung which is attributed to the contraction at the right apex. It is more likely that this dulness is due to bronchial node enlargement.

In addition to anterior and posterior percussion, Bing²³ outlines the apices according to Goldscheider, whose method differs from König's, in that he percusses in sagittal lines, i. e., parallel with the vertebral column, and he finds that enlargements of the bronchial nodes cause a narrowing of the normal resonant isthmus at the extreme summit of the lung, due to external dislocation of the inner border of normal resonance. This method of percussion requires much greater skill than either the anterior or posterior method and the dulness so obtained is certainly infrequent with nodes but slightly enlarged. Bing believes that the slight degree of apical dulness sometimes met with in children with adenoids is due in reality to enlarged bronchial nodes rather than to the induration collapse to which it is commonly attributed.

30. Fetterolf and Norris: *Am. Jour. Med. Sc.*, 1912, cxliii, 637.

31. Boggs: *Arch. Int. Med.*, 1911, viii, 659.

AUSCULTATION

As with the lungs and heart, so with the bronchial nodes, auscultation is our most valuable method of examination. There is nothing characteristic in the respiratory murmur over the lungs with moderate enlargement of the bronchial nodes. Normal breath-sounds are the rule. As the nodes become larger the vesicular equality diminishes and is sometimes entirely replaced by tubular breathing usually most marked in the interscapular space. Again with very large nodes the breathing may be diminished owing to the small amount of air entering the lung. In one instance I noticed a diminution of the respiratory murmur associated with an increased whisper. Several years ago D'Espine³² drew attention to the fact that in children whispered bronchophony normally ceased at the seventh cervical vertebra, but that with enlargement of the bronchial nodes it extended downward over the upper thoracic. D'Espine has had several post-mortem confirmations of the trustworthiness of this sign. The occasional occurrence of bronchophony in the interscapular space was noted by Laennec³³ in "*lean children*," but he apparently did not appreciate its significance. D'Espine suggests auscultating over the upper thoracic spine while the patient whispers "three-thirty-three." In young children I found this sentence rather involved, so I substituted the word "tree," which is repeated three times (*tree, tree, tree*). If the bell of the stethoscope is placed directly over the lower cervical spines and the patient whispers this sentence, one observes that the final "e" persists for an appreciable time after the voice has ceased. Only this post-phonial sound is of significance; the mere persistence of vocal resonance is not. As has been said, this normally does not occur below the cervical vertebræ in children, and in adults it usually stops at the same level, but with a sonorous voice it may apparently persist as low as the third or fourth thoracic vertebræ without significance, unless it is marked and heard at one or both sides of the vertebræ. The area over which the whispered voice may be heard varies greatly. Sometimes it is limited strictly to the vertebral spine, but usually it extends to one or both sides. Frequently it is heard as far out as the border of the scapula and quite often it follows the line of the left bronchus. Twice in adults I have heard it as low as the sacrum. In another adult it was so marked to the left of the upper thoracic vertebræ that except for the absence of râles a cavity was suggested. In this case it eventually completely disappeared. Two patients in whom I had noted this sign have come to autopsy. In one, a woman of 66, the sign was present over the upper fourth thoracic vertebræ and also slightly to the right thereof. The expiration was also

32. D'Espine: Bull. de l'acad. de méd., Paris, 1907, lvii, 167.

33. Laennec: Epoch Making Contributions to Medicine, Surgery and the Allied Sciences, Camac, Philadelphia, 1909, p. 125.

somewhat increased at the right apex. No lesion was found at either apex, but there was an enlarged node about the size of an English walnut just above the right bronchus (Fig 9). In the other case, an adult male, the increased whisper was heard throughout the interscapular space and was most marked at the left to the mid-thoracic vertebræ. A few scattered tubercles were found in the lung and the marked enlargement of the bronchial nodes is shown in Figure 10 and Figure 11. Strong flexion of the head will sometimes increase this sign. One possible explanation of the whispered bronchophony is that the bronchial quality of the voice is conducted to the vertebræ by the swollen glands and when heard to the side is due to rib conduction. It is quite likely, however, that the transmission may sometimes be a direct one. Increased vocal resonance is normally present over the manubrium sterni, but when the anterior group of nodes are swollen whispered bronchophony may be very marked. It was present both anteriorly and posteriorly in a recent case of probable aneurism of the arch of the aorta, due presumably to pressure on the trachea. In infants the character of the cry is substituted for the word "three." In several elderly people with a chronic cough which was subsequently proved to be tuberculosis, I found the whispered bronchophony very marked. Gray³⁴ was the first in this country to call attention to the value of this sign. In a former paper³⁵ I reported whispered bronchophony in eighty out of 168 children. Sixty-six per cent. of those in whom it was present reacted to tuberculin as against 25 per cent. of the others. Since then seventy-five other delicate children have been examined and tuberculin-tested. Whispered bronchophony was present in a little over one-half of the cases, and in these over 79 per cent. gave a positive reaction, while but 50 per cent. of those not giving the sign reacted positively. Whispered bronchophony was sought for in 266 office patients—all adults—most of whom had some symptoms suggestive of tuberculosis. These cases were classified as follows: Active tuberculosis (mostly very early cases), 43 per cent.; latent tuberculosis (healed), 8 per cent.; suspected tuberculosis, 24 per cent.; non-tuberculous, 24 per cent. It was present in 84 per cent. of the active cases and 83 per cent. of the latent; 72 per cent. of the suspected cases and 43 per cent. of the clinically non-tuberculous. If only the cases in whom the sign was very marked at the sides of the vertebræ as well as over the spines had been included in this last group, the percentage would have been considerably less.

It is interesting to compare these auscultatory results with the percussorial results of Bing³⁶ and Gunmach.³⁶ The former found inter-

34. Gray: *Proc. Nat. Assoc. for Study and Prevent. of Tuberculosis*, 1908, iv, 300.

35. Stoll, H. F.: *Am. Jour. Med. Sc.*, 1911, cxli, 83.

36. Gunmach: Quoted by Krämer (Note 4).

scapular dulness in 75 per cent. of his tuberculous cases, while Gunmach obtained it in 80 per cent. Roch³⁷ investigated the value of this sign in adults and concluded that it was of a great deal of significance when heard over the midthoracic region, but of questionable value when not heard below the level of the third or fourth thoracic spines. A note of dissent comes from Kidd,³⁸ who asserts that interscapular dulness is never present unless the lung is affected, and from the examination of fifty-one patients, mostly adults, he concludes that whispered bronchophony is not a trustworthy guide as to the size of the bronchial nodes. Inasmuch, however, as he considered the sign positive in adults when present only over the second or third thoracic spines, his dissension loses much of its weight.

The venous hum heard over the manubrium sterni when the head is strongly extended and described by Eustice Smith³⁹ as being indicative of enlarged tracheo-bronchial nodes, does not seem to be a sign of much value.

Material weight is lent to the diagnosis of bronchial node tumor when both dulness and bronchophony are present. But from the physical signs alone the nature of the swelling cannot be determined. Even when the tuberculin test is positive, we have to fall back on the symptoms to ascertain whether we are dealing with clinical tuberculosis, which needs immediate treatment, or only an anatomic lesion which requires temperance in all things.

THE X-RAY

(Drs. A. C. Heublein, O. R. Witter and H. F. Stoll)

We will first consider the shadows produced by the normal thoracic viscera before describing those of the swollen lymph-nodes. The large central shadow has been likened by D'Oelsnitz¹⁴ to a bottle (or distillatory flask), the body being caused by the heart and the neck by the vertebral column and mediastinal contents. The hilus shadow is fan-shaped and radiates from the central shadow for about 4 cm. to the right of the fifth, sixth and seventh thoracic vertebræ. This is caused by the wall of the stem bronchus, the pulmonary vessels with their contained blood, the lymphatic and fibrous tissue. Fine markings, due to the bronchial walls, blood-vessels and lymphatics are seen in the lung fields radiating toward the periphery. Slightly to the right of the vertebral column between the heart and the clavicle, one normally sees a faint veil-like shadow about 1 cm. wide (Fig. 12 "N"). Dunham and Boardman⁴⁰ demonstrated that the superior vena cava played an important part in its protection. In the case of mitral stenosis with tricuspid insufficiency already referred to,

37. Roch: *Semaine m d.*, 1911, xxxi, 85.

38. Kidd: *Lancet*, London, 1911, i, 561.

39. Smith: *Wasting Diseases of Childhood*, London, 1899, p. 309.

this shadow was considerably widened, especially at its lower end where it joined the cardiac outline. This substantiates their contention. The consensus of opinion as to the ability of the x-ray to show bronchial nodes is as follows: Normal glands never cast shadows; calcified glands always do; cheesy glands almost always do. Swollen, but not cheesy, glands usually do. As a result of the comparison of the physical signs with the x-ray plate in over seventy-five cases which Drs. A. C. Heublein and O. R. Witter were kind enough to take for me, we have concluded that, as a rule, the earliest x-ray evidence of enlarged bronchial nodes is a shadow seen to the right of the vertebral column. It is in the position normally occupied by the superior vena cava, but is of greater density and protrudes further into the lung field. This shadow extends from about the tip of the third cartilage upward toward the clavicle and gives an increased width to the root of the lung. The lower border may terminate at the heart, or it may be seen through the cardiac shadow extending to a somewhat lower level (Fig. 13). By consulting Figure 1 it will be seen that this region just to the right of the sternum and vertebræ is occupied by the trachea, the peritracheal nodes and the nodes just above the right bronchus. When the enlargement is small, no individual glands are seen, the only thing being noted is the increase in the transverse diameter at the right of the lung already referred to. It is quite likely that the engorgement of the lymph and venous trunks from the pressure of the glands contributes to this shadow. When the nodes attain greater size, the shadow may assume a lobulated appearance (Figs. 14 and 15). The next most common change is seen in the hilus shadow which is enlarged, more dense and may show individual nodes (Fig. 16). They may be of indefinite outline and of little density, or very opaque when calcareous. There may be an increase of the bronchus shadow with no definite hilus glands (Fig. 17). We have rarely seen the infratracheal group in an antero-posterior view because of the intervention of the cardiac shadow. They can be seen, however, in Figure 18. The nodes along the left bronchus are also revealed with difficulty save when calcareous, because of their position behind the heart. It is for this reason that the right oblique position should be used, as the post-cardiac glands will then be seen between the heart and the vertebral column. The heavy trunks which radiate from the hilus shadow are usually seen, but we can give no opinion as to the interweaving of the fine linear markings in the periphery of the lung-fields as described by Dunham and Boardman,⁴⁰ as facilities were lacking for making stereoscopic radiographs at the time this investigation was undertaken. We have observed, however, that clouding of the apices may antedate by some time the development of tubercles.

40. Dunham and Boardman: Bull. Johns Hopkins Hosp., 1911. xxii, 229.

From our experience we conclude that the *x*-ray is of great value in detecting bronchial node enlargements. The healed nodes are recognized by their small size and dense shadow. We feel that the *x*-ray cannot distinguish between actively tuberculous glands and those in which the disease is "latent."

We have had no experience with the radiographic appearance of the enlarged thymus but the work of Dr. Selby at the Mayo Clinic, and Ferrand and Chatellin,⁴¹ and of D'Oelsnitz¹⁴ in France, leave no doubt as to its value. As a rule, the thymus shadow is predominantly on the left side and does not have the lobulated appearance often seen with enlargement of the bronchial nodes. The shadow of the intrathoracic thyroid begins at about the upper border of the second costal cartilage, and as it extends upward it widens out. This should not be confused with the shadow of either bronchial nodes or enlarged thymus.

The fluoroscopic examination is very valuable, but does not afford a permanent record capable of careful study.

CONCLUSIONS

1. A moderate enlargement of the bronchial nodes often gives physical signs of sufficient distinctness to render their diagnosis possible by clinical methods alone.

2. The signs are usually most marked in the interscapular space.

3. Tapping percussion will elicit bronchial node dulness that is imperceptible when more force is used.

4. Whispered bronchophony in the interscapular space is the earliest and most valuable sign of swollen bronchial nodes. It is especially significant in children and has almost, if not quite, the same importance in adults.

5. While the spasmodic, brassy cough is quite typical of bronchial node tumor, the diagnosis must sometimes be made in the absence of the cough.

6. An ever-present fatigue, associated with anorexia, afternoon temperature and possibly a slight loss of weight should suggest the possibility of their tuberculous nature.

41. Ferrand and Chatellin: *Bull. Soc. de pédiat. de Paris*, 1911, No. 4, 164.

A GRAPHIC CHART METHOD OF STUDYING AND TEACHING THE PRINCIPLES OF INFANT FEEDING

WITH SPECIAL REFERENCE TO THE IMPORTANCE OF THE ENERGY LINE *

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I wish to present a method which I have been using with considerable satisfaction in teaching the principles of infantile nutrition, a graphic chart method which supplements previous instruction. The chart is simple, easily understood and records the weight variations, the energy line, which indicates how much food the infant needs, the food blocks, which show how much food has been given and retained, and presents a graphic representation of the number and character of the stools. Various other happenings of the day can also be indicated. Thus the chart forms a complete summary of the case for each day. A few explanations will be necessary.

The chart is arranged for daily records for eight weeks with room for a gain of 4 pounds. The spaces between the ordinates represent days, each abscissa represents 2 ounces, between the abscissæ 1 ounce. A gram column parallels the pound column. The calorie column may be started with each abscissa representing either 10 or 20 calories and is usually begun on an even number approximately corresponding to the caloric requirement 1 pound below the entrance weight, in order to allow for weight drops, etc.

Plotting the Energy Line.—This line is constructed from the infant's weight, 45 calories per pound during the first six months of life, gradually declining to 40 or 36 calories during the latter months of the first year.

Plotting the Food Line.—The caloric value of the food is calculated in the usual way. After the student has become thoroughly familiar with this computation he is given a table of the caloric values of one ounce of the various foods used in the ward. (Table 1.) The amount of food in calories ingested and retained is charted. (See Chart 9.)

Charting the Stools.—A series of symbols are used. These may be varied as one desires. The usual ones employed and which the nurses and

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*Read by title at the meeting of the American Pediatric Society, Hot Springs, Va., May, 1912.

students use with readiness are the ones indicated in the stool column. Such combinations of these symbols as the following may be made:

The first symbol indicates a hard stool with curds; alkaline in reaction; the second a liquid stool with curds, mucus and blood; acid reaction; the third an extra sign for any other type of stool.



The chart when completed for the day is a representation of the so-called percentage and caloric methods. Both of which must figure in

TABLE 1.—THE CALORIC VALUE OF ONE OUNCE OF THE VARIOUS MODIFIED MILK FORMULÆ AND FOODS USED IN PALMER MEMORIAL WARD

Formula, Per Cent.			Calories From			
F	S	P	Fat	Sugar	Protein	Total
1	5	0.5	2.79	6.15	0.61	9.55
1.5	5	0.5	4.18	6.15	0.61	10.95
1.5	5	0.75	4.18	6.15	0.922	11.235
1.5	5	1	4.18	6.15	1.23	11.56
1.5	5	1.5	4.18	6.15	1.845	12.17
1.5	5	2	4.18	6.15	2.46	12.79
2	5	0.5	5.58	6.15	0.615	12.34
2	5	0.75	5.58	6.15	0.922	12.05
2	5	1	5.58	6.15	1.23	12.96
2	5	1.5	5.58	6.15	1.84	13.57
2	5	2	5.58	6.15	2.46	14.19
2.5	5	1	6.97	6.15	1.23	14.35
2.5	5	1.5	6.97	6.15	1.84	14.96
2.5	5	2	6.97	6.15	2.46	15.58
3	5	1	8.37	6.15	1.23	15.75
3	5	1.5	8.37	6.15	1.84	16.36
3	5	2	8.37	6.15	2.46	16.98
3	6	1	8.37	7.38	1.23	16.98
3	6	1.5	8.37	7.38	1.84	17.59
3	6	2	8.37	7.38	2.46	18.21
3	5	2.5	8.37	6.15	3.07	17.59
3	5	3	8.37	6.15	3.69	18.21
3.5	5	3	9.76	6.15	3.69	19.60
4	5	3	11.16	6.15	3.69	21.01
Whole milk						21.01
Milk Sugar						13.00
Cow's milk						21.01
Woman's milk						20.5
Skim milk						12.0
Whey						6.0
Buttermilk, approximately						5.0
Precipitated casein, approximately						15.0
Eiweissmilk, approximately						11.0*
Keller's malt-soup, approximately						24.0
Oat flakes, dry, approximately						116.0
Barley flour, dry, approximately						103.0

*The caloric value of *Eiweissmilk* varies 11 and 15 calories per ounce, depending on the percentage of fat in the whole milk and the quality of the buttermilk.

the proper feeding of an infant. There has been so much said about the advantages of one method over the other that I usually begin my work in infant feeding by illustrating the foundation that has been laid in this country by American masters whose names are so familiar to all of us. America has been in no way behind in the development of a knowledge of infantile nutrition. Chart 1 illustrates how closely we have come to the needs of the body as attested by the energy line. I have plotted the weight-curve of a normal bottle-fed baby (taken from Holt) and the maximum amount of food in calories used as a routine by those who follow the percentage feeding scheme. (Arranged from Holt's table.) The gain in weight is seen to follow feeding above the energy line. A chart plotted with the optimum amount of food generally prescribed would bring the food line from 20 to 70 calories above the energy line. It will be seen that infants fed by this scheme have not been underfed, and it should also be stated that the proportion of each food constituent has been carefully adjusted.

TABLE 2.—PROTEIN REQUIREMENTS PER KILO OF BODY-WEIGHT

Age	Required Grams of Protein per		
	Kg. Body-Wght	Pound	Ounce
2 Weeks	1.5	0.68	0.0425
2 Weeks	1.5	0.68	0.0425
3	2.0	0.90	0.056
4	2.5	1.10	0.0687
2 to 12 months ..	2.5-3.3	1.10-1.5	0.093

The most important point to impress on the student is the basic protein requirement of the body. By a previous special study of metabolism as related to infantile growth and development, the student has become acquainted with this basic or minimum protein requirement. He is now taught how to put this into practice by means of the chart. Chart 2 illustrates a simple case. By use of the accompanying table (2) he determines the number of grams of protein required and from this it becomes a simple matter to determine the percentage. He then chooses 5 or 6 per cent. sugar as a constant and makes up the balance of his calories from fat. In the present case the infant has been started on a 2-6-1.5 mixture. The protein has been gradually increased to 1.75 per cent. or 2 per cent. and the fat by steps from 2 to 3 per cent. As the protein is the tissue builder it is placed as the foundation stone in the food block. The daily quantity of food is readily determined as follows:

TABLE 3.—CHART MAKING EXERCISE, BABY A., CASE 1

Date	Weights from Birth		Food from Birth		Stools from Birth
	Pounds	Ounces	Formula	Ounces	
June 1	7	10	2 normal
2	2
3	7	8	3
4	6% sugar whey	10	3
5	4
6	7	5	3
7	1½-5-½	20	3
8	1 normal, 1 curd
9	7	8	2 normal
10	3
11	7	10	2
12	2
13	7	11	3
14	2-5-¾	30	3
15	3
16	7	14	2 normal, 1 with curds
17	3 normal
18	8	3
19	2
20	8	4	4
21	2
22	2
23	2
24	8	6	2-5-1	30	2
25	2
26	2
27	8	10	3 normal, 1 with curds
28	3
29	2
30	2
July 1	8	14	2
2	2
3	2
4	8	14	1
5	2½-6-1	31	1
6	3 normal, 3 with curds
7	8	14	2 normal, 1 liquid curds
8	3 with curds
9	2 curd, 1 liquid, with curds
10	8	12	2 4
11	6 liquid with curds
12	8	8	27	4
13	3
14	2 with curds, 1 normal
15	8	10	3 normal
16	2
17	2
18	9	2	28	3
19	3
20	2
21	9	6	2
22	3
23	30	3
24	9	10	2
25	2
26	2

TABLE 4.—CHART MAKING EXERCISE, BABY B., CASE 2

Date	Weights		Temperature		Food		Stools
	Pds.	Ounces	M	E	Formula	Ounces	
July 21	12	12	98.4	98.8	3-6-1½	36	2 normal
22	98.	98.6	2 normal
23	98.2	98.4	3 normal
24	13	..	97.8	98.4	2 normal
25	98.4	99.	3 normal
26	98.6	98.6	2 normal
27	13	4	98.4	98.8	2 normal
28	98.	98.6	1 normal, 1 liquid
29	13	5	98.8	98.4	2 liquid, acid
30	98.6	99.	2 semi-liquid, mushy
31	98.	98.8	1 semi-liquid, 1 normal
August 1	13	5	98.6	98.8	2 normal
2	98.	98.6	2 hard
3	13	4	98.4	98.6	3 semi-liquid, mushy
4	98.	98.9	4 semi-liquid, mushy
5	13	4	98.4	98.8	4 semi-liquid, mushy
6	13	6	98.8	98.6	5 semi-liquid, mushy
7	13	1	98.6	98.4	31½	3 semi-liquid, mushy
8	12	11	97.6	98.6	3 semi-liquid, mushy
9	12	6	96.8	97.4	2 semi-liquid, 1 liquid
10	12	6	95.	97.6	33	2 semi-liquid
11	12	8	97.4	98.4	34	1 semi-liquid, 1 normal
12	12	9	96.4	96.2	34½	2 normal
13	12	9	96.2	95.6	1 hard
14	12	4	96.2	96.2	4 semi-liquid, mushy
15	12	2	96.	96.6	5 semi-liquid, mushy
16	11	14	95.2	96.6	Tea	5 semi-liquid
17	11	10	96.4	97.4	B. M.	24	3 semi-liquid, 1 liquid
18	11	11	97.2	97.8	4 liquid with curds
19	11	12	96.8	97.	3-6-1½	25 boiled	4 liquid with curds
20	11	12	95.8	97.2	3 semi-liquid with curds
21	11	13	97.	98.	3 semi-liquid
22	11	13	98.	98.4	2 semi-liquid
23	12	3	98.	98.4	2 semi-liquid
24	12	9	98.4	98.6	30 boiled	1 semi-liquid, 1 normal
25	12	13	98.4	98.8	2 normal
26	12	14	98.6*	99.	2 hard
27	12	15	2 hard
28	12	15	2 hard
29	13	4	31 boiled	2 normal, 1 hard
30	13	5	3 normal
31	13	5	2 normal
Sept'ber 1	2 normal
2	13	6	34½ past	1 hard
3	2 normal
4	13	9	3 normal
5	3 normal
6	2 normal
7	13	10	2 normal
8	1 hard, 1 normal
9	Fresh	3 normal
10	13	12	2 normal
11	36 fresh	2 normal
12	13	14	3 normal
13	2 normal
14	14	2 normal
			3 normal

*Temperature normal thereafter. B. M. = Buttermilk.

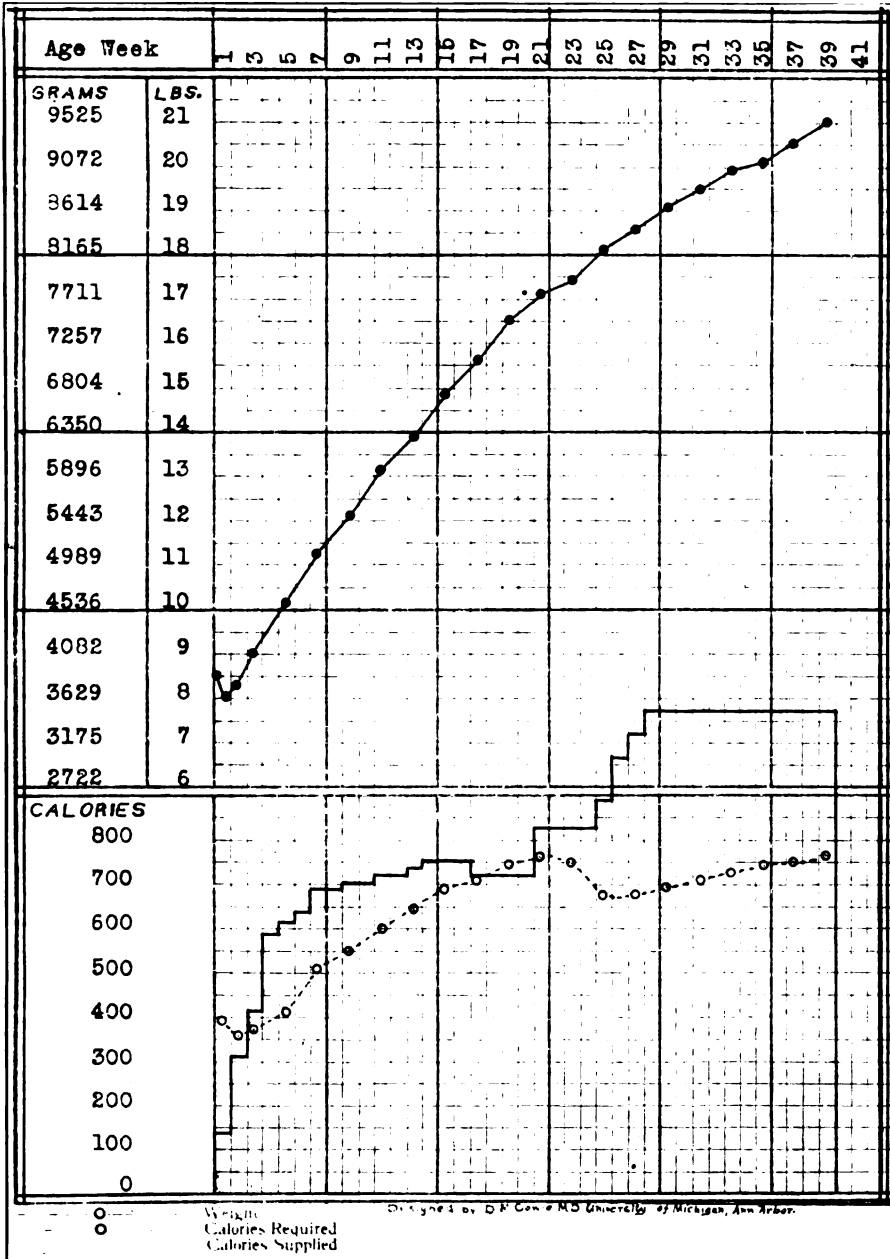


Chart 1.—This chart shows the average weight curve of a normal bottle fed infant, the energy line (calories of food required), and the amount of food (in calories) supplied by the maximum percentage formulæ quite generally employed by pediatricians in the United States. The chart further shows how correctly American children have been fed by the percentage method without reference to the "caloric method."

NAME Baby A. Case 1.

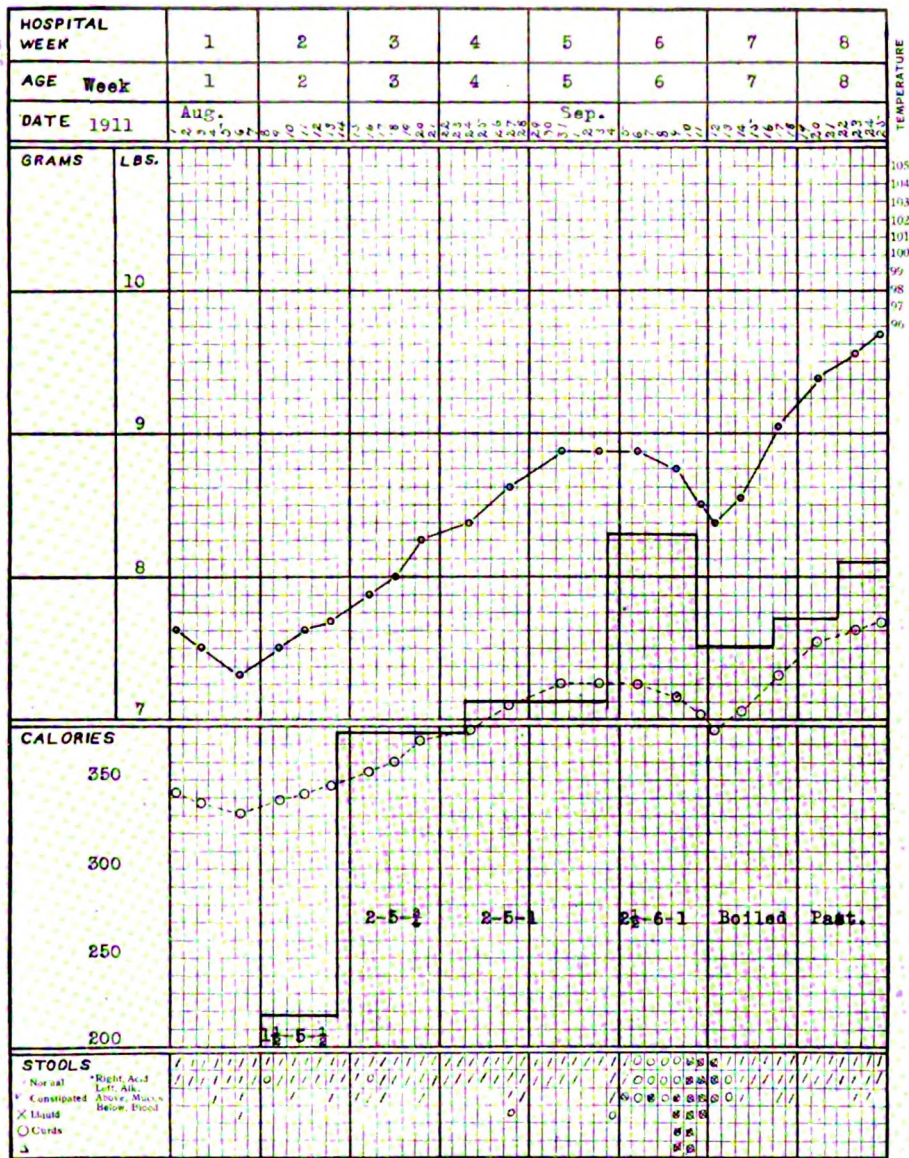


Chart 3.— $1\frac{1}{2}$ -5- $\frac{1}{2}$ etc. = $1\frac{1}{2}$ per cent. fat, 5 per cent. sugar, $\frac{1}{2}$ per cent. proteid.

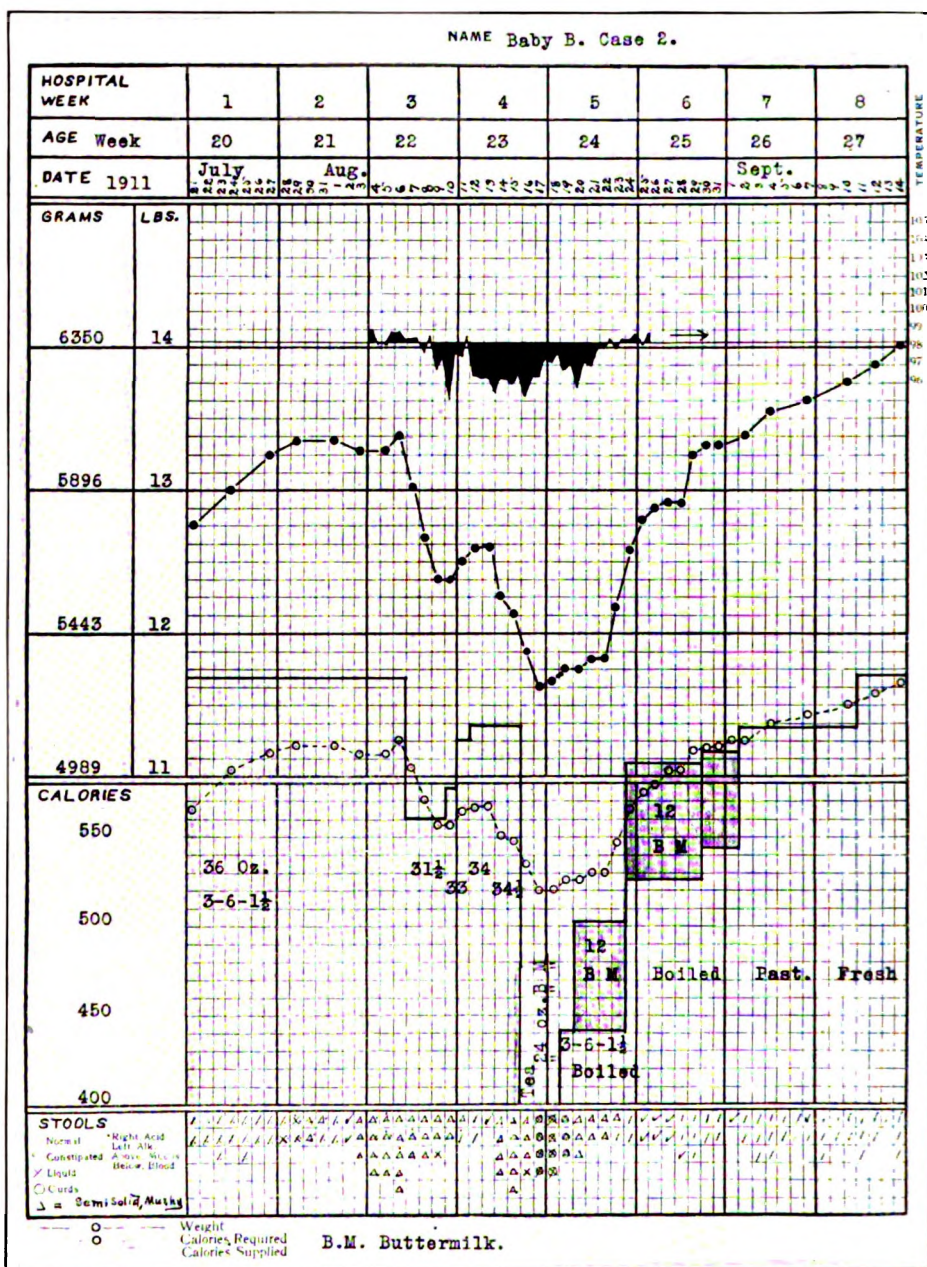


Chart 4.

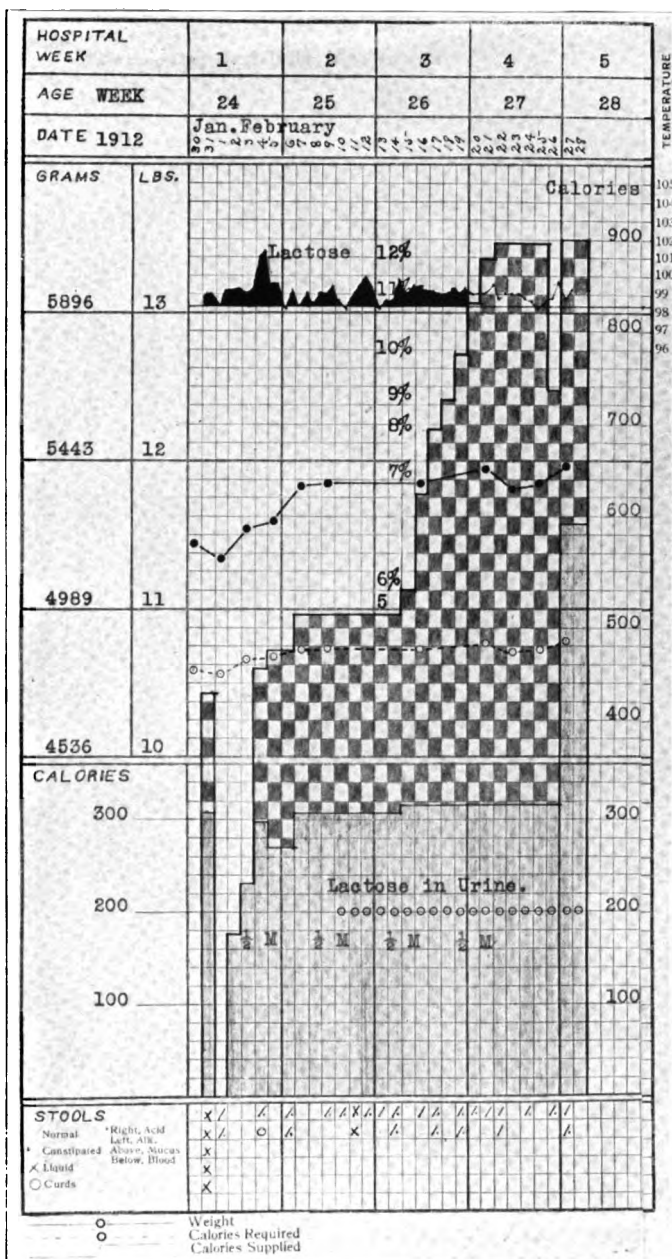


Chart 5.—Illustrating high sugar tolerance; $\frac{1}{2}$ M = half milk. The checkered portion shows amount of lactose added to the $\frac{1}{2}$ M.

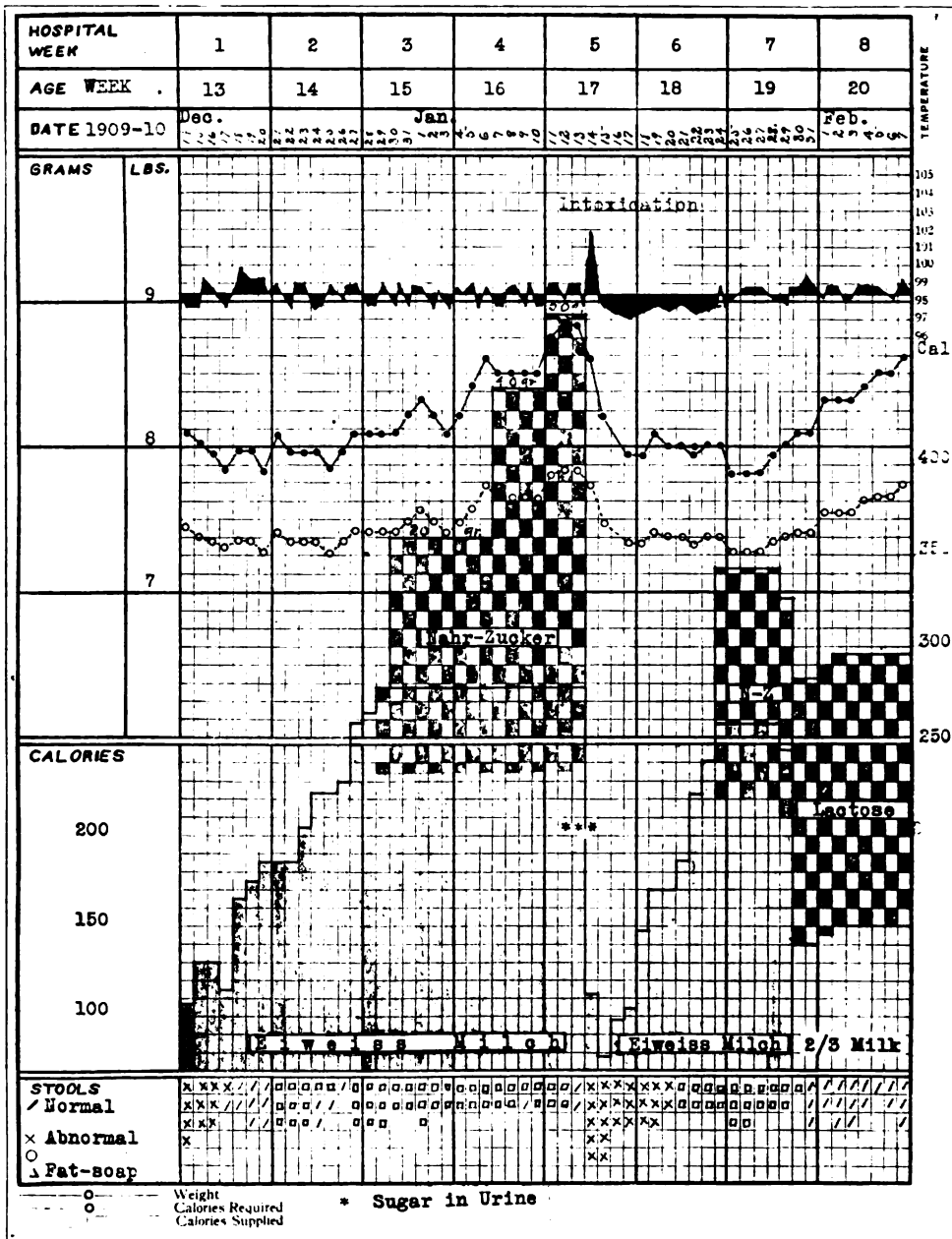


Chart 6.—Illustrating low sugar tolerance and resulting slight intoxication. The checkered portion below the *Eiweissmilch* line gives the approximate amount of sugar supplied in this food, above the line the amount of sugar added. The caloric value of the *Eiweissmilch* was doubtless higher than here estimated. Adopted from Finkelstein and Meyer. See text.

In the present case, one ounce of 2-6-1.5 mixture has a caloric value of 14.8; 385 calories are required to bring the food up to the energy line. This number divided by 14.8 gives approximately 26 ounces, as the total amount of food. The food for a new patient is usually started a little below the line and later is pushed, as a routine, 30 or 40 calories above the line, to the approximate point of optimum tolerance.

Isabel K.

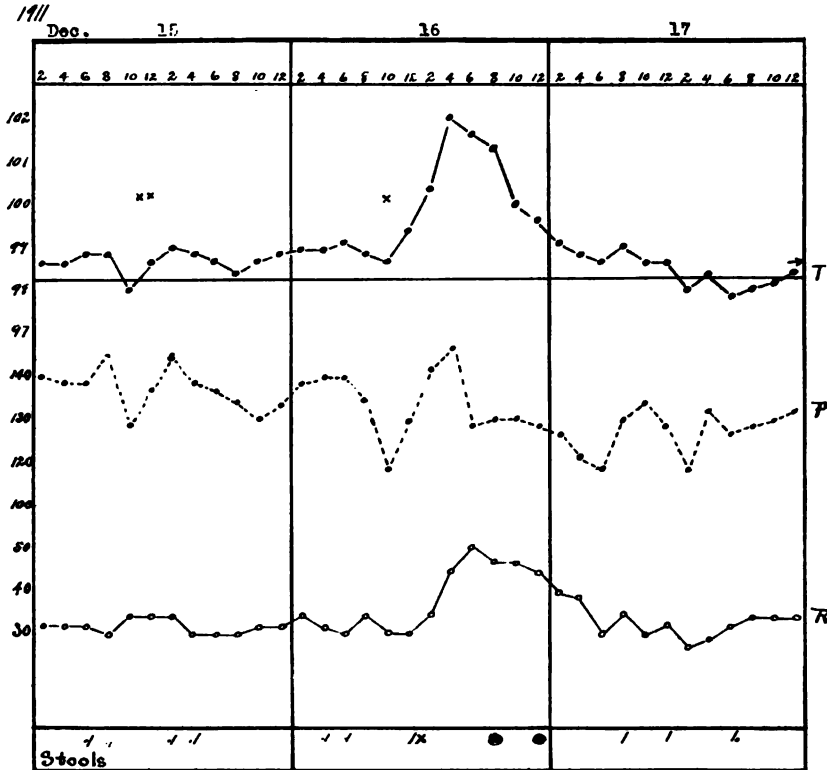


Chart 7.—Temperature, pulse and respiration curves in the case of Isabel K., a girl-baby, 10 weeks old, with normal digestion and normal stools. December 15 points marked xx 50 grams of 1 per cent. NaCl solution were given by gavage, December 16 at point x 100 grams of a 4 per cent. NaCl solution were given by gavage. There was no pyrogenic reaction following 1 gram of NaCl, but distinct reaction following 4 grams. There was also a marked respiratory increase and a pulse reaction. The stools increased in number and character after the ingestion of the salt solution.

The student is now given a number of exercises to work out in order to familiarize himself with the keeping of a chart. He is furnished with blank charts, pencils, etc., and an instructor to explain all the steps taken. He first plots the weight-curve. From this he constructs his energy line. By the time he has figured this line for one chart it becomes an easy task

for him to calculate caloric requirements. Next comes the plotting of the food blocks and the stools. The class is kept together on the first chart to avoid confusion. That is, all the members of the section start each division of the chart at the same time. The chart finished, the student discusses in writing the possible causes of the weight-drop and makes a diagnosis. The completion of the chart takes almost invariably one and a half hours.

Chart 3 results from the first exercise and represents a case of simple dyspepsia from overfeeding.

Chart 4 results from the second exercise and represents a case of marasmus or the so-called decomposition. It has taken this infant eight weeks to gain 1 pound. This gain is accomplished by feeding close to the energy line. It illustrates low food tolerance. The primary drop in the third week is overcome by lowering the food below the energy line. A substantial gain is made with partial improvement in the stool, but when

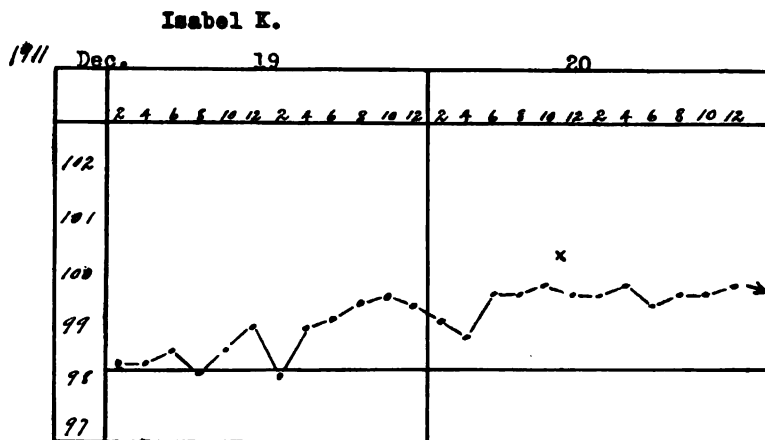


Chart 8.—Temperature curve in case of Isabel K. At point marked x 100 c.c. of 4 per cent. sodium bicarbonate solution were given by gavage. No pyrogenic reaction followed. The elevation of temperature was due to developing chicken-pox.

the food goes 50 calories above the line a relapse takes place. The further treatment of the case is self-explanatory. These two cases are almost entirely diagrammatic and are not given out as actual cases. Further exercises are given out to be done by the student at his home.

We next take up the study of sugar tolerance. This is illustrated by Chart 5, which represents an actual study of a case by the section.

In this chart a very marked sugar (lactose) tolerance is shown. In this normal infant on the seventeenth day, after a week of stationary weight, gradually increasing percentages of sugar were added, as indicated on the chart. When 5, 6, 7, 8, 9, 10, 11 and 12 per cent. are indicated,

approximately 48, 53, 78, 90, 117, 126, 141 and 146 grams of lactose are supplied. While there was no increase in the weight, as might have been expected for a short time, there was no marked fall, no rise in temperature, no increase in the frequency of the stools and no sugar appeared in the urine. The rise in temperature during the first week was due to circumcision.

In Chart 6 just the opposite condition is recorded. On the addition of only 50 grams of sugar, or when the sugar in the food is approximately 7 per cent., distinct symptoms of intoxication are produced. Coincident with sharp rise in temperature there are a number of abnormal stools, a decided drop in weight and the occurrence of sugar in the urine. With a reduction in the food, particularly in the sugar content, the weight ceases to drop and does not rise again until the food block nears the energy line. In this case a substantial gain is recorded with the food 80 calories below the energy line.

I have constructed this chart (5) from one of Finkelstein and Meyer's cases.¹ The stools are supplied but they conform to the characteristics exhibited in mild cases of sugar intoxication and in infants fed on *Eiweissmilch*. In this case preceding the records here presented, during the twelfth week, while the infant was being fed buttermilk plus 5 per cent. lactose (making in all about 7.5 per cent. lactose) symptoms of dyspepsia developed with slight elevation of temperature. The improvement following the treatment with *Eiweissmilch* is indicated. There is first a period of seventeen days of practically stationary weight when with the addition of 20 grams Nährzucker, bringing the food line up to the energy line, the weight begins to increase until the point of intolerance is reached by the addition of 50 grams of sugar which brings the food 85 calories above the energy line. The characteristics of sugar intoxication and its treatment according to Finkelstein are indicated on the daily records which follow. With the exception of the weight-curve the chart bears little resemblance to the original from which the data was taken and converted into English terms.

This case brings up the subject of the effect of salts in infant feeding. During the period of buttermilk feeding in the case just mentioned there developed along with the dyspepsia a slight fever. It is not difficult to figure out the amount of salts the infant got during this time and one might reason that the dyspepsia and the intoxication following it some weeks later may have been due to injury of the intestinal epithelium by these salts. I therefore present some illustrations of the effect of feeding varying amounts of common salt to healthy babies. The following case will serve as an example. (Charts 7 and 8.)

1. Finkelstein and Meyer: Case 24, Curve 10, *Jahrb. f. Kinderh.*, lxxi, series 3, xxi.

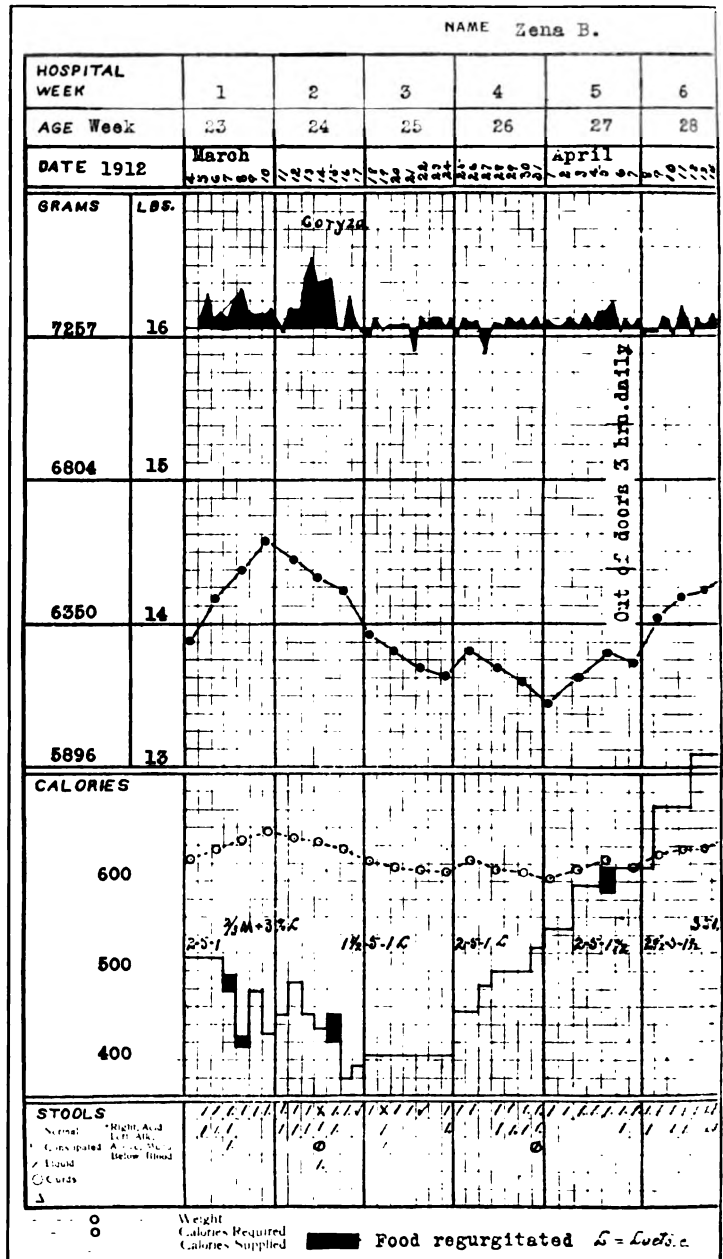
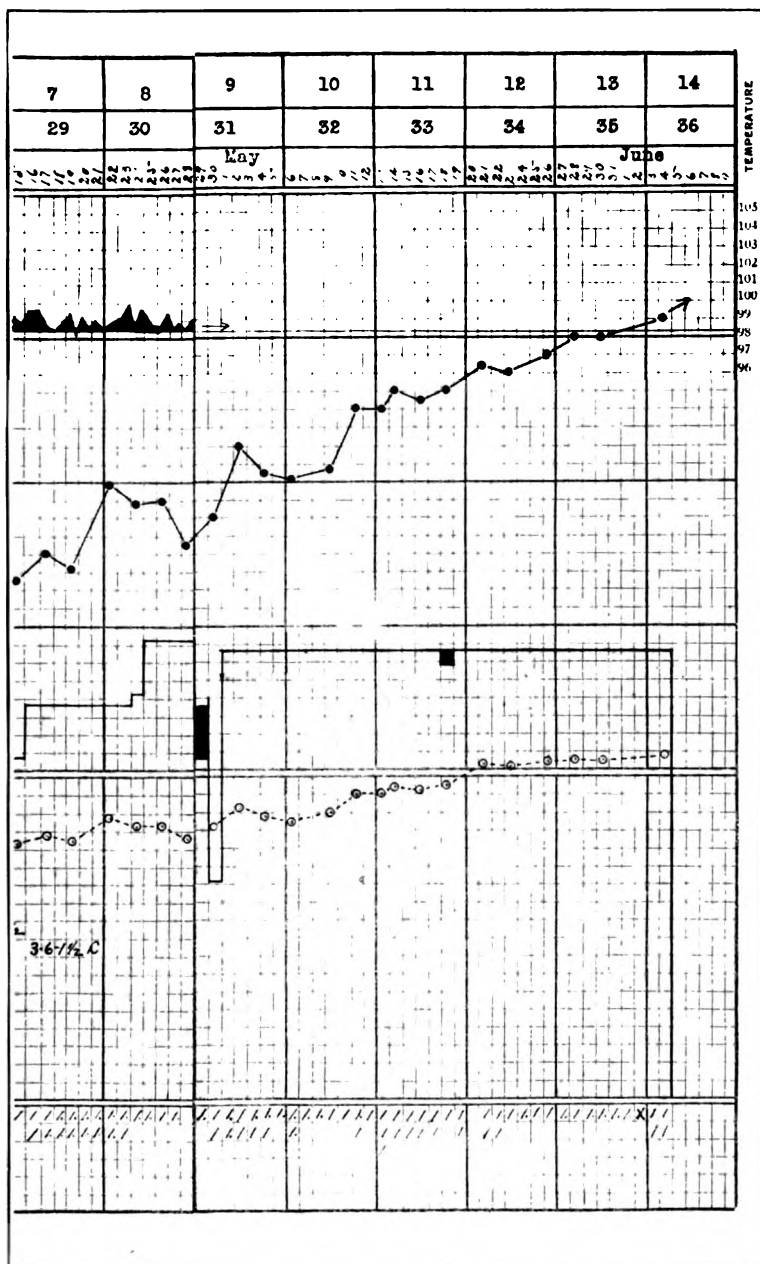


Chart 9.—A good illustration of the value of the energy lines (calori dressings for club feet. In later weighing



quired). The gain during the first week is largely due to adjustment of plaster weight of dressings accounted for.

Isabel K., girl baby 10 weeks old, with normal digestion and normal stools. On December 15 after a stationary temperature for eight hours and normal temperature prior to that time she is given by means of gavage in two doses an hour apart 100 grams of a 1 per cent. sodium chlorid solution, which represents 1 gram of salt. No pyrogenic reaction follows. Twenty-four hours later 100 grams of a 4 per cent. solution of sodium chlorid is given in one dose, by gavage. This represents 4 grams of salt. A distinct and marked pyrogenic reaction develops, reaching its height in six hours, declining to normal in eighteen to twenty hours. During the pyrogenic phase there is also a marked respiratory increase and pulse reaction as well as an increase in the number, and a change in the character of the stools. This phenomenon occurs with such great regularity when the proper amount of salt is given that it is very easy of demonstration before the class.

By Chart 8, and others which are not necessary to print, the specificity of the salts is illustrated. In this same case several days later the effect of sodium combination with the non-halogen element carbon is tried. Four grams of sodium bicarbonate produces no pyrogenic reaction and at this point it is shown that in milk the halogen combinations of sodium alone produce the pyrogenic reaction. It is therefore the sodium chlorid in the milk which is responsible for this reaction and is a constituent of the infant's food which should be considered in cases of obscure fever, diarrhea, etc., as well as the sugar and other constituents of the food. The subject of water retention by the sodium salts is also suggested at this time.

The student is now ready to go into the wards and follow his cases through. Since developing this chart method an interest in even the usually uninteresting cases has been awakened. The student feels that he is really doing something and although his visits night and morning to the ward are kept track of, the tendency to bolt has practically disappeared. I might record many charts like Chart 9, which have been kept by the students. This case shows the importance of carefully watching hospital cases. It is really difficult to do this without a graphic chart of some kind.

Zena B. (Chart 9), club foot, was referred to the pediatric department for nourishment. She was in one of the surgical wards in another building and away from the direct observation of the nurse in charge of the feeding cases. The intern had prescribed a 2-5-1 formula. The child made a good gain in its first week in hospital. On the fourth day the intern tried a simple milk dilution, bringing the sugar up to approximately 6 per cent. by an addition of 3 per cent. lactose. About this time the child developed a coryza with slightly abnormal stools, fever, and loss of weight. The fever subsided after four days, the stools became normal after one day but the weight continued to fall. On the twenty-first day the child was brought to the Palmer ward (Ped. Dept.) and a chart was started (Chart 9). It will be observed that the infant was being fed far below the energy line. The food was gradually increased to the energy line and pushed above it with the results seen in the chart. The black areas represent the number of calories lost through regurgitation. The marked regurgitation on April 29

2. Dividing the dose as in the control makes no difference in the result.

following declining weight after marked increase in the food and refusing of the total quantity made us fear the development of a dyspepsia from over-feeding; consequently on the following day the child was fed below the energy line. No bad symptoms developing, the food was again pushed to just a little below the former point, with only one day of slight regurgitation in six weeks. The temperatures are all rectal. We find that a large per cent of our babies run a temperature like the one plotted, from the third hospital week on, without any discoverable cause. It may be well to state that the salt content in our percentage formulæ is never excessive. This chart is an exact copy of the one made by the student in charge of the case.

It is not the purpose of this paper to demonstrate any classification of the digestive disturbances of infancy. It is apparent how a chart can be used to illustrate the various causes of stationary, declining and increasing weight with their attendant symptoms and signs.

The lessons we learn from practical use of a graphic chart are that changes in weight are usually explained at a glance; that a child cannot make substantial gain on feeding below its caloric needs; that he may often make a loss by feeding far above the line and that when strict attention is given to this point, with proper adjustment of percentages and attention to fundamental principles, most cases improve. There are instances in which the very best of care and thought cannot suffice to bring about improvement.

HELMINTHIASIS IN CHILDREN *

W. W. MURPHY, M.D.

CHICAGO

The subject of helminthiasis in children has been revived in the literature in the last few years. The statistics as given in the text-books have been drawn from the clinical work in hospitals and private practice and are naturally inaccurate, as many of the cases show no symptoms and the clinical examinations have not been controlled by careful laboratory examination. In the last few years, however, there have been two investigations reported, based on thoroughly scientific work. The earlier work, that of Stiles and Garrison, reported in 1906, gives a thorough digest of the voluminous literature and was practically the only report on the subject in the United States until Schloss reported his series of 310 cases from the clinics of three hospitals in New York. The latter report was the direct stimulus for the present investigation. The percentage of infections (28.57 per cent.) reported in this paper being so much higher than clinical reports would indicate, gave rise to the question whether the percentage rate was really lower among the cases in the Chicago clinics, or whether the routine examinations in the laboratory had been inadequate. With these questions in mind, the present investigation was started.

The work was carried on in the laboratory of the Michael Reese Hospital and extended over a period of eight months. The cases were taken from patients in the Children's Ward in this hospital. They were taken consecutively as they entered without regard to whether they showed any symptoms referable to infection with parasites.

The purpose of the work as outlined was primarily to determine: First, the frequency of infection with intestinal worms in children between the ages of 2 and 12 years; second, the species of parasites harbored; and third, the relative frequency of infection with the different species of parasites.

The question of the constancy of eosinophilia in infections with intestinal worms, the number of cases that show the usual symptoms of helminthiasis and the nature of those symptoms, were considered secondarily only, as the cases were all patients admitted to the wards for some affection other than helminthiasis.

*From the department of Pediatrics and the Laboratories of the Michael Reese Hospital, Chicago.

The method of examination used for diagnosis was a careful macroscopic and microscopic examination of the feces for the parasites, parts or segments of the parasites, their ova or larvæ, and the results reported are based on such findings. As often as it was possible, the stools were obtained after a purge with calomel and in every case that was doubtful or positive the duplicate examinations were after a thorough calomel purge. An average of two and a half stools was obtained from every case, though in thirty-four of the cases it was impossible to obtain more than one stool, owing to the patient disappearing from our observation, or for similar reasons. The technic of the microscopic examination consisted of an emulsion of a small portion, approximately 10 to 15 grams, of the thoroughly mixed feces in 30 c.c. of distilled water, varying the amount as necessary to make a translucent mixture, and from

TABLE SHOWING COMMON SYMPTOMS IN HELMINTHIASIS

No.	Age	Sex	Race	Nation- ality	Intercur- rent Disease	Para- site	Gastroin- testinal	Nervous	Loss in Weight	Skin
1	6	F.	R. J.	U. S.	Chorea	T. t.	Appetite poor	Very nervous
2	10	M.	R. J.	U. S.	Mitral and Aortic Insuf- ficiency	T. t.	Appetite poor abd. distress	Restless
3	8	M.	R. J.	U. S.	Endocar- ditis	T. t.
4	4	M.	R. J.	U. S.	Leg burn	Asc.l
5	2½	F.	R. J.	U. S.	Chronic Osteo	Asc.l
6	6	M.	R. J.	U. S.	Helmin- thiasis	Tae.s	Appetite poor	Slightly	Slight	Purpura hemor- rhagica
7	4	M.	R. J.	U. S.	Burns	Tri.i	Restless

this emulsion not less than five preparations were made from each stool by placing a drop on a glass slide and covering with a cover slip. These were then studied very carefully with both the two-thirds and one-sixth objectives. In all, stools from 102 children were examined. The age limit was set at 12 years, as the intention was to confine the investigation entirely to children.

In regard to the nationality, a word must be said, as it may have a direct bearing on the significance and interpretation of the results. The patients were almost entirely of Russian Jewish parentage, although nearly without exception of American birth. The fact that all the statistics of the foreign reports show a very much higher percentage of infections than any of the reports for the United States would make this point vital in interpreting this report as an index to conditions in the United States.

A very large majority of the cases were taken from the charity wards of the hospital. They represent, therefore, the children from the homes of the poorer classes, where the housing conditions and mode of living are far from good. The questions of occupation, place of residence, rural or city, and previous residence, have all been answered.

Stools were examined, then, from 102 of these patients under 12 years of age and the following results were obtained: Of the 102 children, seven, or 6.86 per cent., harbored parasites, and one case was infected with two species of parasites, making a total of eight infections, or 7.84 per cent. Of these, the *Trichiuris trichiura* was present four times, or in 3.92 per cent. of the cases; the *Ascaris lumbricoides* in two, or in 1.96 per cent. of the cases, and one case each of infection with *Tænia saginata* and *Trichimonas intestinalis*.

Since these seven positive cases were in the hospital with a diagnosis other than helminthiasis, it is difficult to attribute any one symptom or group of symptoms to the one or the other affection. Further, it follows that the symptoms of the intercurrent diseases being most prominent, may overshadow and obscure the manifestations of infection with intestinal parasites and make the interpretation of these evidences difficult and at best presumptive. In the preceding table have been tabulated the symptoms most commonly attributed to helminthiasis.

The blood-picture in the cases shown in the table was as indicated in the following table:

Number	1	2	3	4	5	6	7
Hemoglobin	78	90	75	not	85	75	85
Eosinophils	0	3	3	made	5	8	0

Taking these up in order, we have first, gastro-intestinal symptoms. Two cases (1 and 2) of infection with *Trichiuris trichiura* and one case (6) with *Tænia saginata* infection, showed slight gastro-intestinal symptoms. In the two latter cases, no other etiology being determinable, it was fair to suppose that the symptoms were referable to the helminthiasis. In only the one case (6) was this proven by the disappearance of the symptoms following the treatment. Nervous symptoms were seen in three cases (1, 2 and 7). These three patients showed restlessness and insomnia, but in none of these could these symptoms be determined as due to the parasites, as the intercurrent disease was more probably the cause. No history or record of appreciable loss of weight was given in any one case except that of the boy harboring a fat tapeworm, and here there was only a moderate loss; in no sense an emaciation. There was but one case which showed any skin manifestations (6). This boy showed

a rather colorless, transparent skin and shortly after the presence of the worm was discovered, he developed purpura hemorrhagica on the elbows, shoulders and back. This lasted only a few days and all evidence of it disappeared after treatment was instituted.

In none of the cases was there any anemia worthy of note. In all, the red count was practically normal and the hemoglobin tests (Dare) showed no case below 75 per cent. and only three below 85 per cent.

Of these seven cases showing infection with parasites, eosinophils were increased in only three cases and in only one of these was there a true eosinophilia. One case infected with the *Trichiurus trichiura* showed a 3 per cent. eosinophilia in a white count of 9,200; one case of *Ascaris* infection, a 2 per cent. eosinophile count in a total count of 20,000 whites, and the third case, the infection with the *Tænia saginata*, showed 8 per cent. eosinophils in a 10,000 total white count. It is easily seen then that in the first two, the *Trichiurus trichiura* infection with 276 eosinophils and in the *Ascaris* infection with 400 eosinophils, there is no increase in the normal number of cells. In the last case, however, the *Tænia saginata* infection, with 800 of these cells, there is the only absolute eosinophilia.

It will be seen then, that there was no constant set of symptoms present that could justly be referred to the helminthiasis. Further, the few symptoms that were evident bore no relation to any particular species of parasites. Case 6, the infection with the fat tape-worm, is the only case that could definitely be stated to have shown anything like a typical text-book picture. Here the poor appetite, some restlessness and irritability, slight loss of weight, mild anemia and the purpura hemorrhagica, with the actual eosinophilia, which disappeared with complete recovery following treatment with santonin and calomel, place this single case beyond question.

SUMMARY

1. Careful examination of the stools from 102 children from 2 to 12 years of age showed that 6.86 per cent. were infected with intestinal parasites. In one case there was a double infection giving a total of eight infections. This low percentage is extremely interesting, especially when compared with those reported by the only two others who have carried on similar investigations. Schloss, of New York, from 280 examinations reports 28.57 per cent., and Stiles and Garrison from 123 examinations report 21.14 per cent.

2. Four (3.92 per cent.) of the cases were *Trichiuris trichiura* infection; two (1.96 per cent.) were *Ascaris lumbricoides* infections; one (.98 per cent.) was a *Tænia saginata*, and one (.98 per cent.) was a *Trichimonas intestinalis*. Comparing these with the relative frequency

shown in other reports, we find the results very similar for these three species of parasites. In all reports, the *Trichiuris trichiura* is three to four times as prevalent as any other parasite. The *Ascaris* is usually mentioned as one of the most common intestinal worms, but the more recent reports seem to disprove this view; the report of Stiles and Garrison showing only .81 per cent. of cases harboring this worm.

3. Only a small percentage of cases infected with intestinal parasites display any obvious symptoms.

4. Eosinophilia was not constant as a symptom of helminthiasis, but when present, it accompanied the other clinical manifestations. Further, its presence bore no relation to the species of parasite harbored.

We realize that the small number of cases and the limits of this series of examinations must be remembered in considering the statistical value of our results. However, we feel that the results justify the conclusion that infection with intestinal parasites is much less frequent among the children of the poorer classes of Chicago than is generally conceded to be the case.

In conclusion, I wish to acknowledge my indebtedness to Dr. Julius H. Hess and to Dr. Solomon Strouse for assistance in the preparation of this report. Also to the members of the pediatric and pathologic staffs of the Michael Reese Hospital for many courtesies shown and to the Department of Pediatrics of Northwestern University Medical School through whom the work was made possible.

Michael Reese Hospital

SERUM TREATMENT OF PNEUMONIA *

ROWLAND GODFREY FREEMAN, M.D.

NEW YORK

During the past few years many new methods for the treatment of that very fatal disease of infancy, pneumonia, have been instituted, but few of these have been markedly successful. Many of us believe that the use of out-of-door air has done more to limit the mortality of pneumonia than has been demonstrated for any of the treatments based on laboratory investigation.

Of the three treatments that come under this class one may mention the use of leukocyte extracts advocated by Dr. Hiss; the use of vaccines either commercial or autogenous, and, finally, the use of the serum.

The leukocyte extract of Hiss has produced some striking results, but has not as yet had sufficient use, I believe, to determine accurately its value. But in a report issued by Hiss and Zinsser¹ in 1908, they describe eight cases with recovery and with a reduction of temperature usually within two to four days after the injections were begun. These injections were repeated daily.

Vaccines, particularly autogenous vaccines, have been considerably used and some of the reports are quite favorable, but Stoner,² who has collected 155 cases of pneumonia, in which the patients were treated with vaccines, reports a mortality of 12.9 per cent. Howland and Hoobler report fifty cases, mostly in young children with bronchopneumonia, and some older ones with lobar pneumonia, treated with stock vaccines, but with no favorable results. A few cases also were treated with autogenous vaccines with similar results.

In going over the literature it has seemed to me that the results obtained from the so-called Romers' serum, a pneumococcus serum, have been in general very favorable. Thus Kriske³ reports ten cases in children from 9 months to 10 years of age in which he noted a distinct improvement after the administration of the serum and all the children recovered. May⁴ reports good results in twenty cases with increased leukocytosis.

* Read at the meeting of the American Pediatric Society, Hot Springs, Va., May, 1912.

1. Hiss and Zinsser: *Jour. Med. Research*, 1908, xix, No. 3, p. 321.

2. Stoner: *A Résumé of Vaccine Therapy*. *Am. Jour. Med. Sc.*, 1911, cxli, 186.

3. Kriske: *Zur Serumtherapie de krupösen Pneumonie*. *Med. Klin.*, 1908, iv, 1881.

4. May: *Ueber die Wirkung des Romerschen Pneumokokken-serums bei der krupösen Pneumonia mit besonderer Berücksichtigung der Leukocyten*. *München. med. Wehrsch.*, 1908, lv, 2140.

Monti⁵ used it in twelve cases with decided benefit, while Knauth,⁶ Linderstern,⁷ Tunher⁸ and Crux⁹ used it with favorable results. Brunning¹⁰ treated six patients with falling temperature, slowing of the pulse and general improvement after the administration of the serum. All these observers used a dosage of about 10 c.c. for children and 20 c.c. for adults.

Morse, in 1903, reported to this society eight cases in which the patients were treated with 5 c.c. of pneumococcus serum every four hours, or about 30 c.c. daily, and concluded that the treatment "had no effect on the duration of the disease, the course of the temperature, the rate of the pulse and respiration or the progress of the local condition. Complications occurred at least as frequently as is usual. Death occurred in an unusually large percentage. The serum, while it apparently did no good, certainly did no harm."

On account of the usually favorable results of treatment with anti-pneumococcus serum it seemed worth while to try it in a series of cases, using alternate cases as controls. This work was undertaken at an institution where the children have poorer reaction to disease than is usual in private practice, and where under any form of treatment many children go on after pneumonia with a condition of unresolved pneumonia which persists for week or months.

The cases admitted to this series were in patients showing a fairly high temperature with good signs in the chest. One of the injected patients had a severe pneumonia complicating measles, another measles-pneumonia being used as a control. This patient showed no good effects from the serum and finally died of general septic conditions and endocarditis. Three patients injected are not included in this paper; two that were moribund when injected and were injected simply to see whether the serum might help them. One of these was rigid and comatose and made no cry when the large needle was thrust into the abdominal wall and died within four hours after the injection. In the other similarly hopeless case the patient died within twenty-four hours after injection. I also injected an adult who recovered.

The first seven of the patients were injected with a simple pneumococcus serum, a large dose, 100 c.c., being injected and in some cases repeated. The injection was done by means of a buret (Fig. 1) made for salvarsan injection and a rubber tube with a glass section near the needle

5. Monti: Arch. f. Kinderh., 1908, x1, 45.

6. Knauth: Deutsch. med. Wehnschr., 1905, No. 12.

7. Linderstern: München. med. Wehnschr., 1905, No. 39.

8. Tunher: Wein. med. Wehnschr., 1906, No. 11.

9. Crux: Zwölf Fälle von Lungenentzündung im Kindesalter mit Romer's Pneumokokkenserum behandelt. Deutsch. med. Wehnschr., 1908, xxxiv, 16.

10. Brunning: Kinderpneumonie und Pneumokokkenheil-serum. Deutsch. med. Wehnschr., 1911, xxxv, 42.

and a very large needle, this being necessary as the blood serum will not flow freely through a small needle. The injections were all made into the anterior abdominal wall and it was found that by keeping the end of the needle in the fascia below the skin and gradually advancing this rather long needle 100 c.c. could be readily delivered with one penetration of the skin. Pressure was made in addition to that of gravity by the use of a rubber bulb attached to the buret.

The first seven patients received 100 c.c. of pneumococcus serum, while the last eight cases received 50 c.c. each of pneumococcus and streptococcus serum. This serum was that of the New York Board of

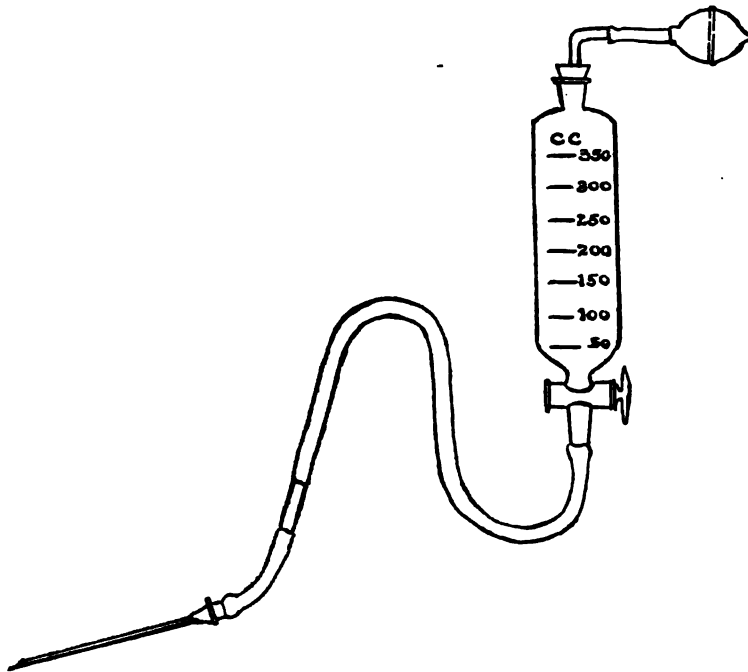


Fig. 1.—Showing apparatus used for injecting antipneumococcus serum.

Health and I am indebted to Drs. Park and Nicoll of this department not only for the serum, but also for advice as to its use.

In none of the cases was there any evidence of irritation at the point of injection. The serum was rapidly absorbed and there was no inflammatory disturbance. In all of the cases, on the other hand, the injections were followed by urticaria, sometimes appearing on the following day, often ten days later, but without fever or general disturbance. In one case in addition to the urticaria an ankle joint was swollen, hot and painful, but this subsided in twenty-four hours and was accompanied by little rise in temperature.

The children injected varied in age from 2 months to 3½ years, the average age being 20 months, while the controls ranged in age from 3½ months to 3½ years, with an average age of 11 months.

As to the effect of the serum, there was in many cases an immediate change in the appearance of the child. Children that looked septic, were apathetic, with anorexia and a pale blotchy complexion, in several cases after the injection, had a good color, were brighter, took the feedings better and seemed much improved, although the condition in the lung was usually unchanged or perhaps spreading.

Before going into the general effect of this treatment I would like to call attention to charts of several cases with marked results, to indicate that in some cases the serum seemed to be of real benefit.

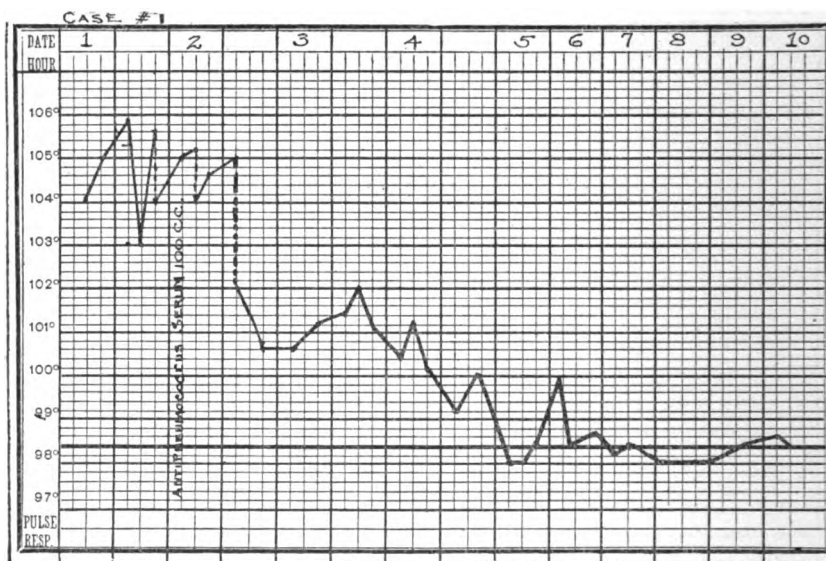


Fig. 2.—Temperature curve in Case 1, showing effect of injection of antipneumococcus serum on second day.

Case 1 was a child that had appeared very sick, the temperature ranging from 103 to 105.8 F., and being 105.2 F. at the time of the injection (Fig. 2). The physical examination showed crepitant râles, increased voice and high-pitched breathing over the upper part of the right lower lobe and over the right middle and upper lobes. After the injection the temperature immediately dropped to 102 F. and then gradually to normal, reaching that point three days after the injection and remaining normal after the fourth day. This injection was made on the second day of the disease and on the following day the signs showed an involvement of the posterior portion of the right lung, while on the third

day after the injection and the fourth day of the disease the signs in the chest cleared up. This was fortunately the first injection case and made a very favorable impression on the people at the institution.

Another striking case was Case 6, in which the patient suddenly had a temperature of 104.1 F., with cough and cyanosis. On examination of the chest in the left subscapular region there was dulness, bronchial breathing, sharp subcrepitant râles, with harsh breathing and crepitant râles lower down, while on the right side there were sibilant râles. After injection the temperature dropped immediately to 99.6 F. (Fig. 3) and never rose, and the signs in the chest gradually cleared up. This seemed like a very wonderful result, but our control patient with no serum did exactly the same thing.

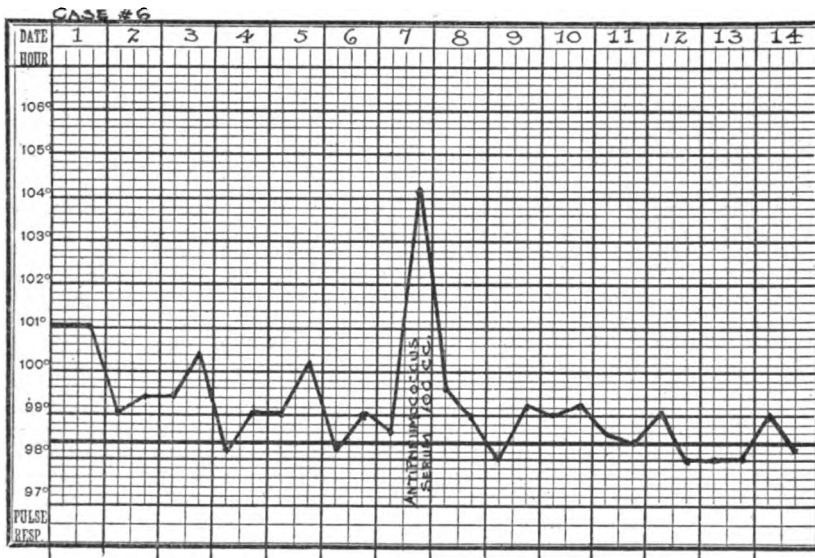


Fig. 3.—Temperature curve in Case 6. Injection of antipneumococcus serum on seventh day.

In Case 10 the child was injected on the fourth day after admission to the hospital, where it was brought on account of convulsions. At the time of injection it had bronchial breathing and crepitant râles over the right upper lobe and the temperature was 102.2 F. (Fig. 4). The temperature reached normal three days after injection. Some signs, however, persisted, but four days after the injection the chest showed only slight dulness at the right apex posteriorly and ten days later when the child was sent out of the hospital the chest was clear.

A very striking case was Case 11, in which the patient had run a steady temperature from 103 to 105 F. (Fig. 5) for four days before injection. At that time the temperature was 104 F., and over the right

lower lobe there was high-pitch respiration and fine râles, and pneumococci were obtained from a throat swab. After injection the temperature rapidly declined and reached normal in three days. In this case the leukocytosis, which was 15,000 at the time of injection, was the same on the following day, but on the second day was reduced to 8,800, while the polynuclear leukocytes changed from 41 per cent. at the time of the injection to 47 per cent.

These cases I have given simply to show that in some cases there was apparently a good reaction from the serum.

The improvement in the well-being of the children has been commented on by other observers and is not always followed by recovery.

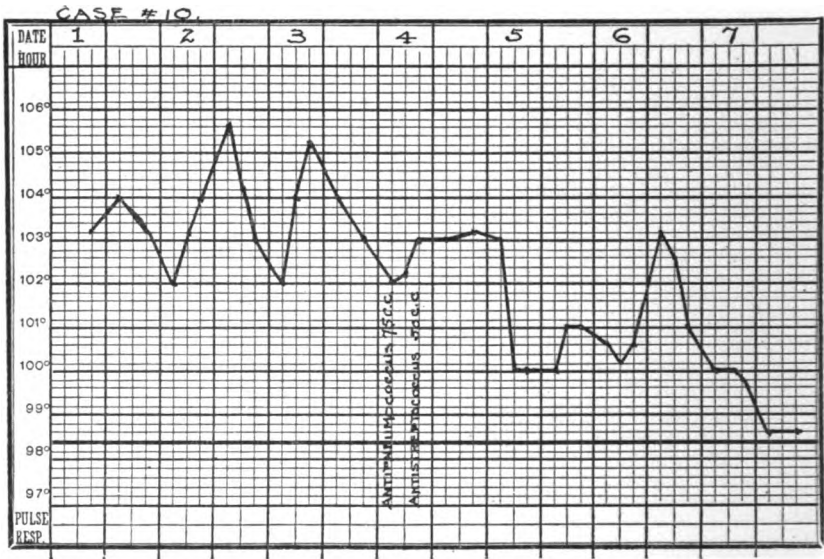


Fig. 4.—Temperature curve in Case 10. Antipneumococcus and antistreptococcus serum on the fourth day.

The effect on the temperature in some cases was marked. In seven cases there was a reduction in temperature after injection, while in eight cases there was no evident effect.

The effect on the process in the lungs was interesting for, as I have said, in some cases in which there seemed to be an improvement in the general condition of the child, the lung condition either showed no improvement or spread. Where there was a marked reduction in temperature from the injection the lung signs did not spread materially and often cleared up quickly.

The effect on the leukocytosis was studied in eleven cases (see table), most of which were injections of combined pneumococcus and strepto-

coccus serum. These showed usually a reduction in the leukocytosis, although in one case the leukocytes increased from 10,000 to 18,000 with a reduction in the polynuclear leukocytes from 70 to 44 per cent. The average of the eleven cases was a reduction in leukocytes from 25,790 to 19,333, and a reduction of polynuclear leukocytes from 67 to 63 per cent. so that the average result is not very striking. A more striking result, but on too few cases to draw any conclusions, is found by examining the three cases in which the counts were made on the third day. These show an average reduction from 29,667 on the first day to 15,300 on the second day, and of 11,933 on the third day, while the polynuclear leukocytes averaged 51 per cent. on each of these days.

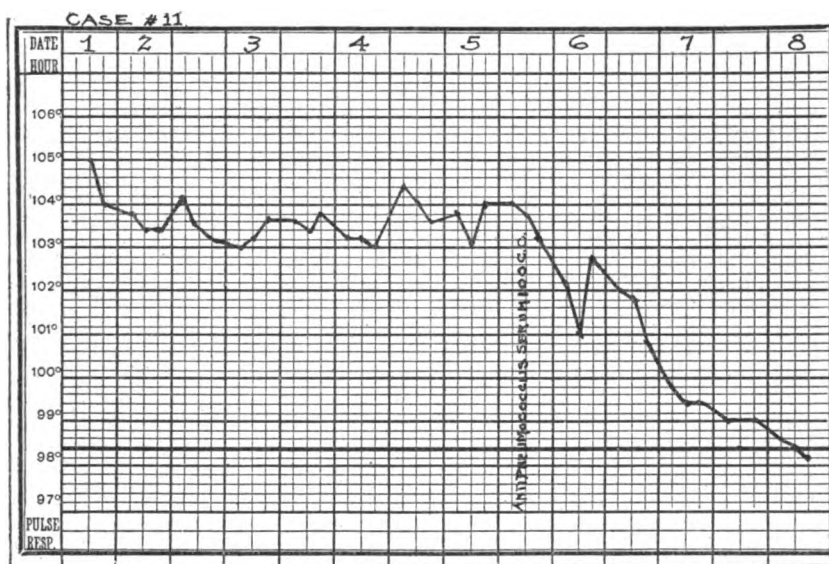


Fig. 5.—Temperature curve in Case 11. Antipneumococcus serum on the fifth day.

The effect of the injections on the duration of the disease may be studied in those patients who recovered. In these it is found that the duration after injection, as shown by fever, varied from one to nine days, the average being $5\frac{1}{3}$ days, and the total average duration of the disease in the patients who recovered being $6\frac{7}{9}$ days, while of the eight control cases the average duration of six was $10\frac{1}{2}$ days, and in two the temperature continued for a very long period.

The crucial test is the effect of the injections on mortality, and in this we cannot make a brilliant showing, for while of the injected patients nine recovered and six died, giving a mortality of 40 per cent.; of the fifteen controls eight recovered and seven died, giving a mortality of 47 per cent. Among the six patients injected with pneumococcus

serum alone there were four recoveries and two deaths, while the controls showed five recoveries and one death. Of the nine patients injected with the pneumococcus and streptococcus serum five recovered and four died, while of the controls of these there were three recoveries and six deaths. Repeated injections in patients who had showed no reaction from the first injection were equally unsuccessful.

RESULT OF BLOOD EXAMINATION AT TIME OF INJECTION AND TWENTY-FOUR HOURS LATER IN ELEVEN CASES

At Time of Injection		One Day Later	
Leukocytes	Percentage of Polynuclear Leukocytes	Leukocytes	Percentage of Polynuclear Leukocytes
58,000	84	18,400	64
17,800	75	11,000	69
24,400	42	21,760	79
14,000	75	14,000	74
15,000	41	15,500	47
26,000	86	17,400	48
34,000	85	36,000	95
10,500	70	18,000	44
16,000	27	12,000	40
40,000	73	21,000	70
28,000	76	27,800	71
<hr/> 283,700	<hr/> 734	<hr/> 212,660	<hr/> 701
*25,790	67	*19,333	63

*Average of the eleven cases.

In conclusion, I would say that the serum injections, while apparently affecting favorably the course of the disease in some cases, appears to have no result in others; that in most cases there appears to be a better reaction on the part of the child after injection than before. It was usually followed by some reduction in leukocytosis, and the percentage of the polynuclear leukocytes was also diminished. In these favorably influenced cases there was little spreading of the disease after injection, and in some a fairly rapid resolution.

The injected patients who lived had a much shorter average course than the controls, and the mortality of the injected cases was slightly less than that of the controls.

The pneumococcus serum presents a safe method of attempting to influence the course of pneumonia in children; the addition of anti-streptococcus serum seems to offer no advantage over the use of the pneumococcus serum alone.

LONG INTERVAL FEEDING OF PREMATURE INFANTS

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MINNEAPOLIS

This paper is not presented for the purpose of proving a theory, but seeks rather to give the practical results of long interval feeding in the fifteen cases here reported.

The method of feeding was not in the beginning deliberately attempted for the purpose of testing its value, but was used in sheer desperation in the first case after failing in attempts to successfully feed the baby according to the usual procedure in the care of premature infants. The results were so striking that a thorough trial was made in the other cases and the results are here given for what they may be worth.

Any one who wishes successfully to care for the premature infant must make himself familiar with the work of Budin and his three great laws:

1. The premature infant must be kept warm.
2. It must be properly nourished.
3. It must be protected from infection.

In following out these rules of Budin an exaggerated importance was originally attached to the incubator, especially in the minds of the laity, but we know now that the *couveuse* is not necessary and that it has its dangers and disadvantages. However, the casting aside of the incubator by many of the best pediatricists and obstetricians was not on account of any desire to get away from the rule that the premature baby must be kept warm, but was only a change of method in obtaining that result. We may also modify our method of feeding without doing violence to our ideas that the nourishment of the premature infant must be wisely regulated. This plays a much more important rôle with the premature than with the full term child, because its food requirements are so much greater according to its weight and because it is so much more easily disturbed by overfeeding. It is almost universally recommended that this increased food requisite be obtained by small frequent feedings of mother's milk, and this was my practice until the experience which led me to try the long interval feeding.

*Read in the Section on Diseases of Children of the American Medical Association, at the Sixty-Third Annual Session, held at Atlantic City, June, 1912.

CASE REPORTS

CASE 1.—Baby girl, G., born Jan. 4, 1911, weight, 2,060 gm.

This is the first case in which the long interval feeding was tried. I had followed up to this time the usual method of small frequent feedings of mother's milk but the baby did not do well. I carefully tried different short intervals as follows: Every two hours, with unsatisfactory results; then one hour and half hour intervals with varying amounts of food, but in spite of previous moderate success with most of my cases of premature babies, I was unable to keep this child from vomiting, having frequent attacks of cyanosis, rapid loss of weight and other marked signs of digestive disturbance and inanition. The infant lost over

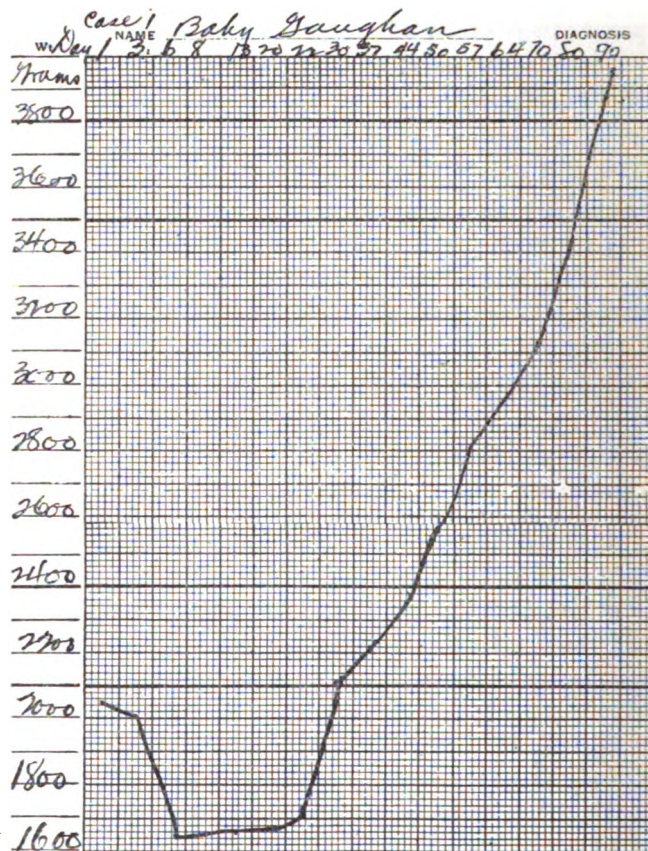


Chart 1.—Weight-Curve in Case 1

400 gm. the first five days of life. I had for some time been a convert to the long interval feeding of mature infants, so in desperation, I ordered on the sixth day four hour intervals, allowing the baby to nurse all it could which in its weakened condition was not much. It weighed at this time 1,651 gm. The change was remarkable; it stopped vomiting at once and had no more attacks of cyanosis. It slept well that night and its progress was continuous. The child gave no anxiety from the sixth to the twenty-second day, when the mother left the hospital and thereafter took entire care of the baby herself, adhering faithfully to the four hour intervals. The weight steadily increased.

Age in Days	Weight, Gm.	Age in Days	Weight, Gm.
1	2,060	37	2,112
3	2,003	44	2,227
6	1,851	50	2,370
8	1,855	57	2,586
13	1,860	64	2,800
20	1,870	70	3,130
22	1,700	80	3,414
30	1,684	90	3,962

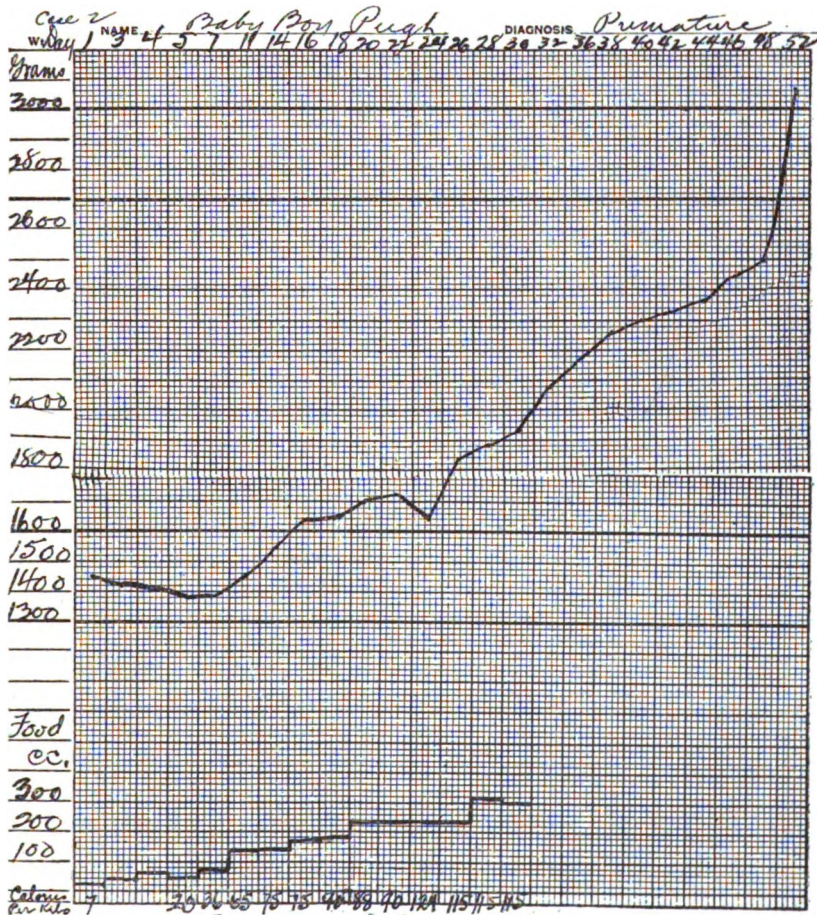


Chart 2.—Weight-Curve in Case 2

CASE 2.—Baby boy P., born June 3, 1911; birth-weight 1,450 gm.

After my experience with Case 1, I determined to try the four-hour interval from the beginning. The baby was given diluted mother's milk for the first four days, was put to the breast every four hours from the first day, but would not nurse much till the fourth day when he took 64 c.c. in twenty-four hours and

thereafter obtained all his nourishment "by the sweat of his own brow." There were no digestive disturbances at any time.

Age in Days	Weight, Gm.	Food per Day, c.c.	Calories per Kilo of Body Weight	Age in Days	Weight, Gm.	Food per Day, c.c.	Calories per Kilo of Body Weight
1	1,450	15	7	26†	1,818	300	115
3	30	..	28	1,889
4*	64	..	30	1,932
5	1,392	40	20	32	2,089
7	1,390	72	36	36	2,188
11	1,448	135	65	38	2,273
14	1,562	167	75	40	2,300
16	1,622	175	75	42	2,314
18	1,655	215	90	44	2,370
20	1,700	215	88	46	2,442
22†	1,720	222	90	48	2,499
24	1,661	310	124	82	3,077

*Nursed.

†Baby taken home.

‡Amounts of food not recorded after this date, but the four-hour interval was maintained.

It is interesting to note in this case that the initial loss was only 60 gm. and that the baby began to gain when receiving only 65 calories of food per kilo of body weight (assuming 700 calories as the value of a liter of mother's milk). It will be noted also that he gained 272 gm. in eleven days, an average of 24 gm. per day on food of a caloric value per kilo of body weight of less than 100. There was a loss of 69 gm. on the twenty-sixth day when the baby was taken home.

CASE 3.—Baby E., born May 29, 1911; thirty weeks' gestation; weight 1,789 gm. Nursed every four hours from the first by a neighbor who came to the house for the first three days, after which the baby was taken half a block to her during the day and milk pumped from her breasts was fed at night. The mother had very little milk when the strong baby of the neighbor was put to the mother's breast to increase the milk secretion. The mother was soon able to nurse her baby at night and by the fifth week was able to furnish sufficient nourishment alone. This baby was weighed only once a week and showed a gain the first week. There probably was an initial loss during this week which was regained. The baby never vomited, never had colic nor a single attack of cyanosis nor digestive disturbance of any kind.

Age in Days	Weight, Gm.	Age in Days	Weight, Gm.
1	1,789	43	2,517
8	1,795	50	2,744
15	1,860	57	2,965
22	1,925	64	3,198
29	2,095	96	4,554
36	2,290		

CASE 4.—Baby boy W., born July 19, 1911. Birth weight 2,329 gm.

The intervals between feedings were four hours from the beginning. For the first four days diluted mother's milk was given; the baby being put to the breast every four hours for attempts at nursing. He nursed some on the fourth day and by the sixth was obtaining all his nourishment from the breast.

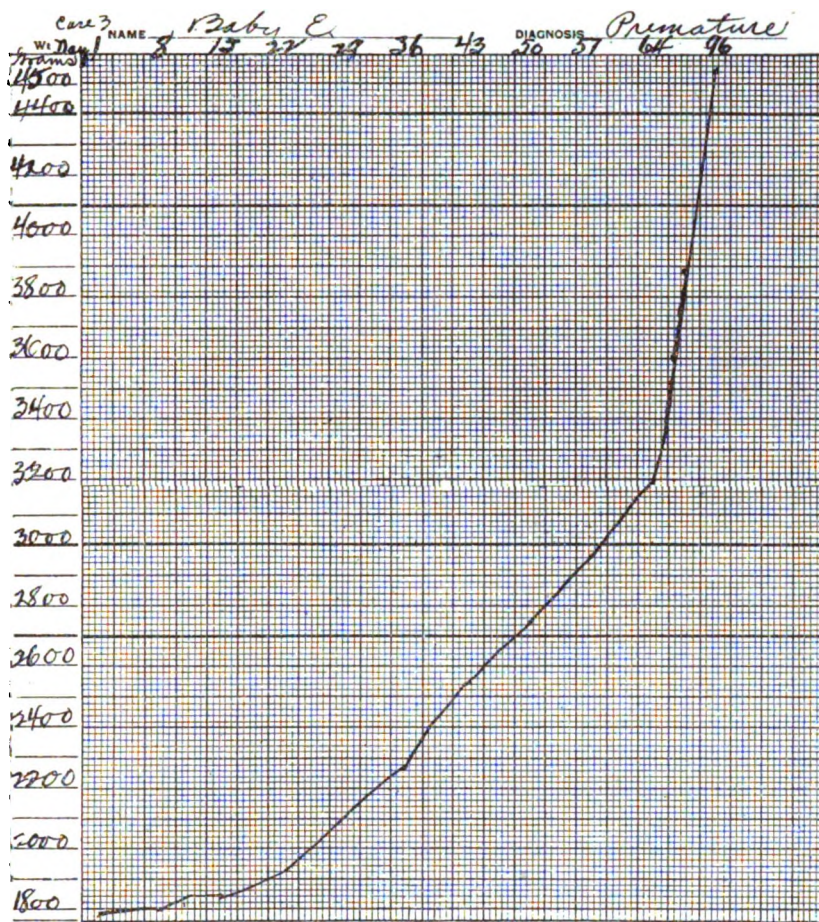


Chart 3.—Weight-Curve in Case 3

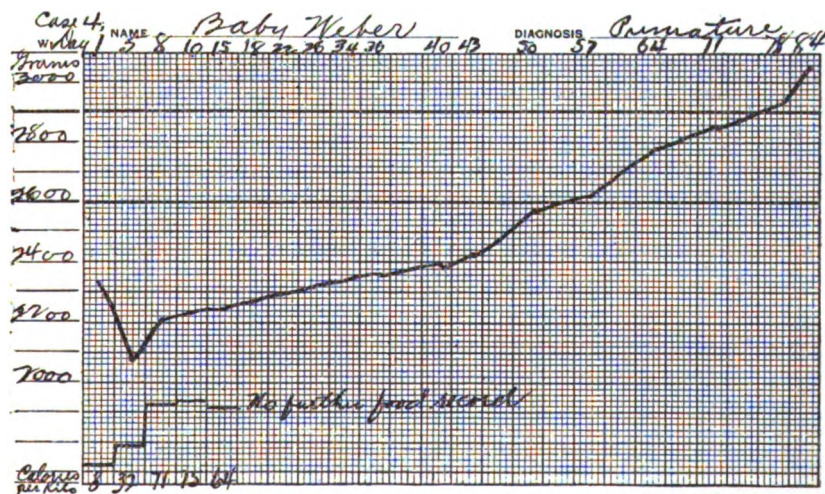


Chart 4.—Weight-Curve in Case 4

Age in Days	Weight, Gm.	Food per Day, c.c.	Calories per Kilo of Body Weight	Age in Days	Weight, Gm.	Food per Day, c.c.	Calories per Kilo of Body Weight
1	2,329	26	8	18†	2,273
2	52	..	22	2,291
3	52	..	26	2,320
4	45	..	29	2,340
5*	2,080	95	32	36	2,357
6	170	..	40	2,386
7†	186	..	43	2,415
8	2,205	225	71	50	2,571
9	165	..	57	2,620
10	2,215	240	75	64	2,780
12	190	..	71	2,845
13	205	..	78	2,912
15	2,245	205	64	84	3,070

*Nursed some.

†Whole amount nursed.

‡Food amount not kept from this date when the mother left the hospital.

The initial loss in this case was 250 gm. but there were no digestive disturbances of any kind. The baby began to gain when the amount of food taken contained 71 calories per kilo of body weight and was still gaining when it was taken home, although the energy quotient had dropped to 64 calories per kilo of weight.

CASE 5.—Baby A., born Oct. 14, 1911.

The mother of this baby had convulsions on the train several hours before arriving in Minneapolis. She was in a comatose state when I delivered her by vaginal cesarean section of a toxic, asphyxiated baby weighing 2,065 gm. It was fed the usual equal parts of mother's milk and sterile water in slowly increasing amounts every four hours, being put to the breast at the same time. It began to nurse a little on the third day, taking a little more each day, but it was two weeks before it obtained all its nourishment by its own efforts.

Age in Days	Weight, Gm.	Food per Day, c.c.	Calories per Kilo of Body Weight	Age in Days	Weight, Gm.	Food per Day, c.c.	Calories per Kilo of Body Weight
1	2,065	15	5	27	2,190	428	136
2	33	..	29	2,270	470	140
4	1,936	37	13	32	2,308	418	126
6	1,945	64	23	34	2,425	488	141
8	1,910	103	37	36	2,515	460	128
12	1,950	178	64	38	2,603	527	141
14	1,975	205	72	41	2,693	598	155
16	2,030	188	64	44	2,925	647	154
18	2,020	155	53	47	3,070	530	119
19	2,015	172	60	49	3,093	693	156
20	2,007	209	72	52	3,190	672	147
21*	2,027	364	120	55	3,330	672	141
22	2,060	335	113	56	3,500	703	140
25	2,130	352	115	58	3,528	620	123

*Wet-nurse employed.

The initial loss in this case was 155 gm. It began to gain on the eleventh day when taking 64 calories of food per kilogram of body weight. It gained 110 gm. on food varying from 64 to 72 calories per kilo in four days, but it lost when the mother's milk began to decrease. On the twentieth day a wet-nurse was employed. The daily intake of food at once jumped from 209 gm. to 364 gm. in twenty-four hours. She was put first to her mother's breast and then to the wet-nurse and allowed to take all she would. The baby of the wet-nurse was used to stimulate



Chart 5.—Weight-Curve in Case 5

the mother's breasts. The calories per kilo of weight went to 120 and never dropped below 113. The gain was now very marked, gaining from 30 gm. to 60 gm. a day, and when the energy quotient went to 140, gained 90 gm. in a day. With these large amounts of food there were no digestive disturbances. This case illustrates that the relatively large amounts of food required by the premature can be obtained and digested even with the long interval.

CASE 6.—Baby boy T., born Dec. 6, 1911, birth weight 1,930 gm. Fed equal parts of mother's milk and sterile water every four hours till it could nurse, which was during the first week.

The initial loss was 270 gm. and was arrested on the fourteenth day. The loss stopped when the baby was receiving only 40 calories of food per kilogram of body weight, and began to gain when receiving 59 calories; it gained steadily, although slowly from the fifteenth to the thirty-seventh day, gaining 275 gm. in the twenty-two days on food running from 60 to 72 calories per kilo of body weight. This may be accounted for by the fact that the baby received a rela-

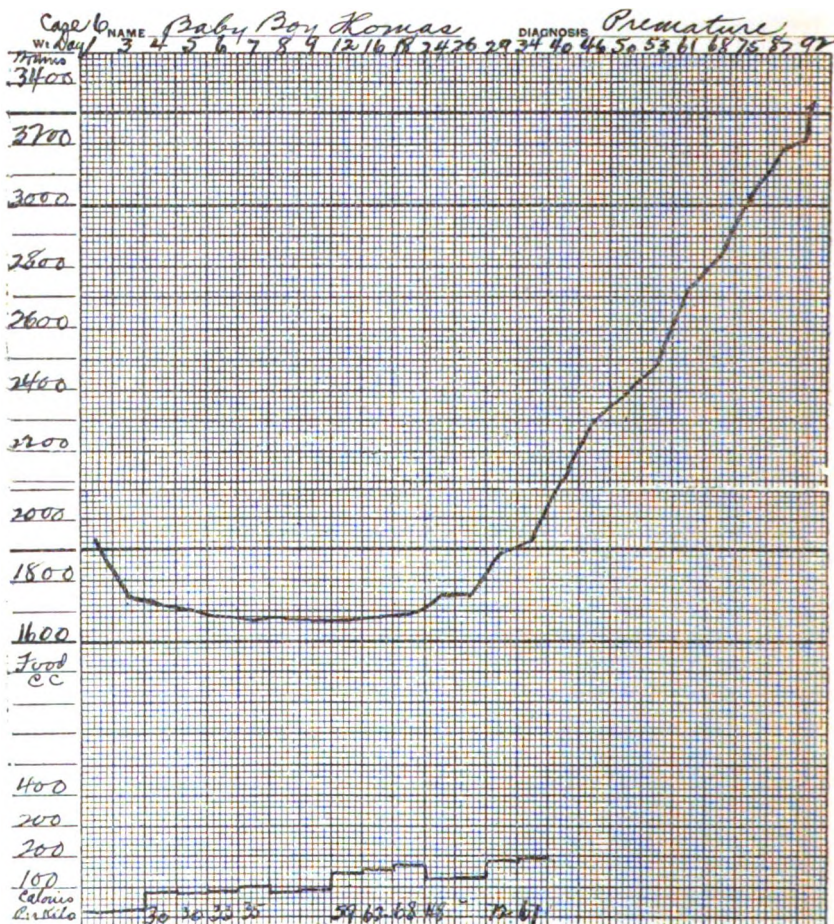


Chart 6.—Weight-Curve in Case 6

tively large amount of water, getting 50 per cent. to 60 per cent. as much water as it did milk. Probably this child would have gained more if it could have had more milk, but the mother did not have an abundance and none was available from other sources; however, the baby gained steadily and after going home the mother's milk increased and from that time on gained rapidly. There never was any digestive disturbance, vomiting or cyanosis. I wonder if this baby would have done as well if it had received less water or been fed more frequently.

Age in Days	Weight, Gm.	Food per Day, c.c.	Calories per Kilo of Body Weight	Age in Days	Weight, Gm.	Food per Day, c.c.	Calories per Kilo of Body Weight
1	1,930	24	8	20	120	..
2	57	..	21	115	..
3	1,740	59	23	23	120	..
4	1,720	90	30	24	1,752	120	48
5	1,700	80	33	25	120	50
6	1,678	85	35	26	1,746	125	..
7	1,665	98	41	28	1,650	176	72
8	1,670	80	33	29	1,888	180	67
9	1,660	89	38	32	1,925	180	65
10	1,660	95	40	34	1,935	185	67
11	1,660	110	46	40*	2,100
12	1,660	140	59	46	2,300
13	1,670	140	58	50	2,385
14	1,670	135	56	53	2,485
15	1,675	143	59	61	2,730
16	1,675	148	62	68	2,868
17	1,685	168	69	75	3,029
18	1,685	165	68	82	3,190
19	123	..	92	3,337

*No record of amount of food after this date; intervals of feeding four hours.

CASE 7.—Baby girl A., born Oct. 17, 1911. Premature delivery at the University of Minnesota Hospital on account of severe infection of the mother's face after extraction of a tooth.

Age in Days	Weight, Gm.	Food per Day, c.c.	Calories per Kilo of Body Weight	Age in Days	Weight, Gm.	Food per Day, c.c.	Calories per Kilo of Body Weight
1*	1,835	28†	1,820	...	37
2	15	..	30	1,880
3**	35	..	31	1,885
6†	1,710	39	16	33	1,850
8	1,685	92	33	35	1,855
10	1,675	123	51	36	1,870
11	1,695	140	51	37	1,860
14††	1,695	95	39	38	1,890
18	1,710	50	2,050
20‡	1,775	152	60	60	2,300
22§	1,840	120	45	70	2,560
24	1,845	100	..	80	2,730
25§	1,855	120	45	97	2,805
27	1,870	100	37				

*Unable to swallow or nurse, fed through nostrils.

**Swallowed readily, vomited, nursed from bottle.

†Nursed a little and fed up to amount recorded.

††Nursed entire amount.

‡Nursed, 85 gm.

§Vomited.

¶Nursed poorly. No human milk available from other source. Human milk brought to hospital from distance by grandmother.

Discharged from hospital. The baby was carried some distance to a neighbor who nursed her every four hours. After three weeks the neighbor could not nurse the baby longer so the baby was taken to the service of Dr. Sedgwick at the University of Minnesota Free Dispensary where she was given the following formula:

One-third raw milk and two-thirds sugar solution (5 per cent.).

Dr. Sedgwick being also a believer in the long interval feeding the four-hour interval was maintained. The next two cases are reported to me by my colleague in the Department of Obstetrics and Gynecology in the University of Minnesota, Dr. F. L. Adair, who is also a believer in the long interval feeding of premature infants.

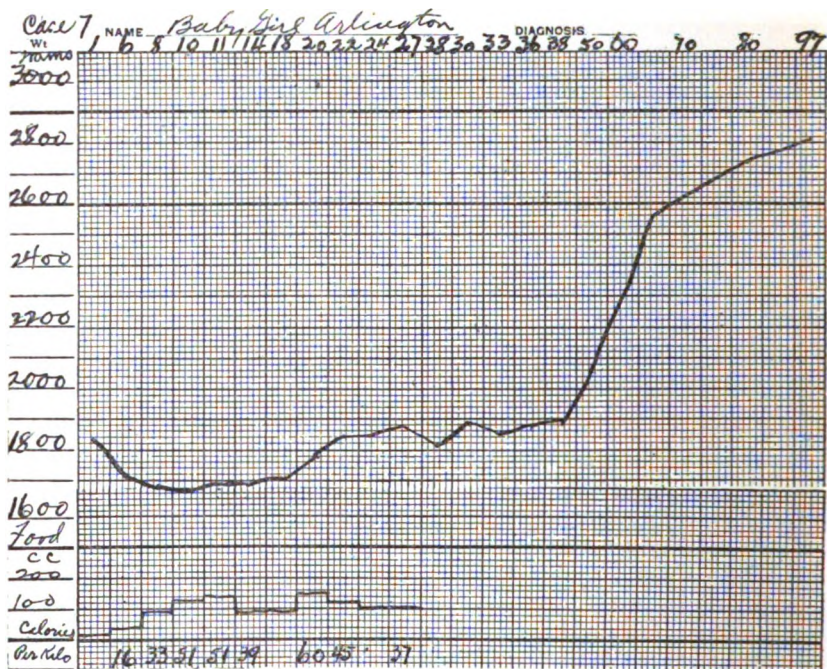


Chart 7.—Weight-Curve in Case 7

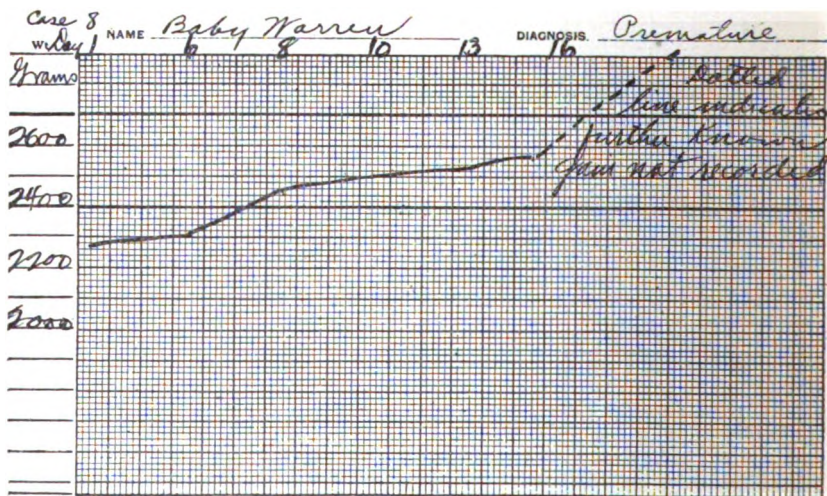


Chart 8.—Weight-Curve in Case 8

CASE 8.—Baby W., born June 27; weight 2,272 gm. Fed every four hours.

Age in Days	Weight, Gm.	Age in Days	Weight, Gm.
1	2,272	10	2,500
6	2,300	13	2,528
8	2,457	16	2,570

No further records are available but it is known that this baby continued to gain without interruption and was entirely free from any digestive troubles.

CASE 9.—Baby Champion, born October 13, weight 1,477 gm.

Age in Days	Weight	Food, c.c.	Age in Days	Weight	Food, c.c.
1	1,477	..	8	1,477	..
2*	11	1,477	..
3†	11	16	1,533	..
5‡	15	19	1,533	..
7§	26	1,874	..

*Would not nurse.

†11 c.c. fed. Nursed well.

‡15 c.c. fed and nursed well.

§Nursed till satisfied.

No further record, but know that the baby continued to gain, had no complications and became a normal, healthy infant.

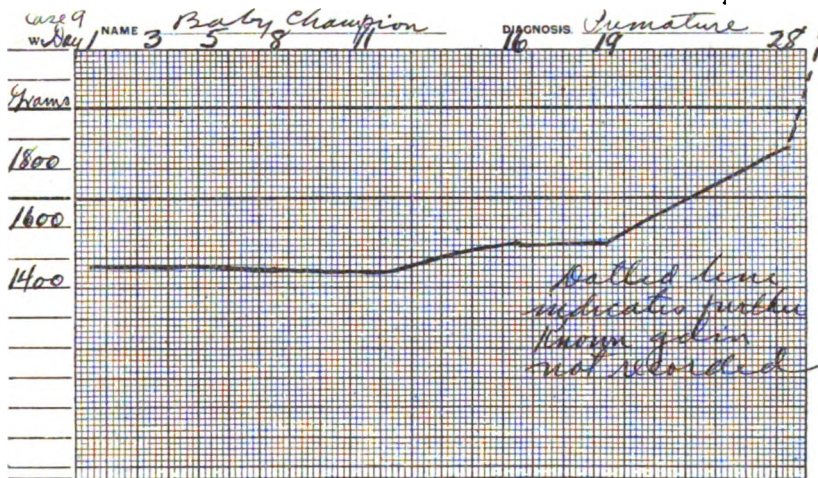


Chart 9.—Weight-Curve in Case 9

The following six cases were observed by my colleague, Dr. F. W. Schlutz, of the department of pediatrics in the University of Minnesota. He studied them in the Auguste Victoria Haus in Charlottenburg, Berlin, under the direction of Keller, who with Czerny, is a firm believer in the long interval feeding of premature infants.

CASE 10.—Elfride P., one of twins, born Sept. 13, 1909; birth-weight 1,680 gm.; fed breast milk every five hours from birth. At first the milk was pumped and fed, but the baby was nursing by the end of the second week.

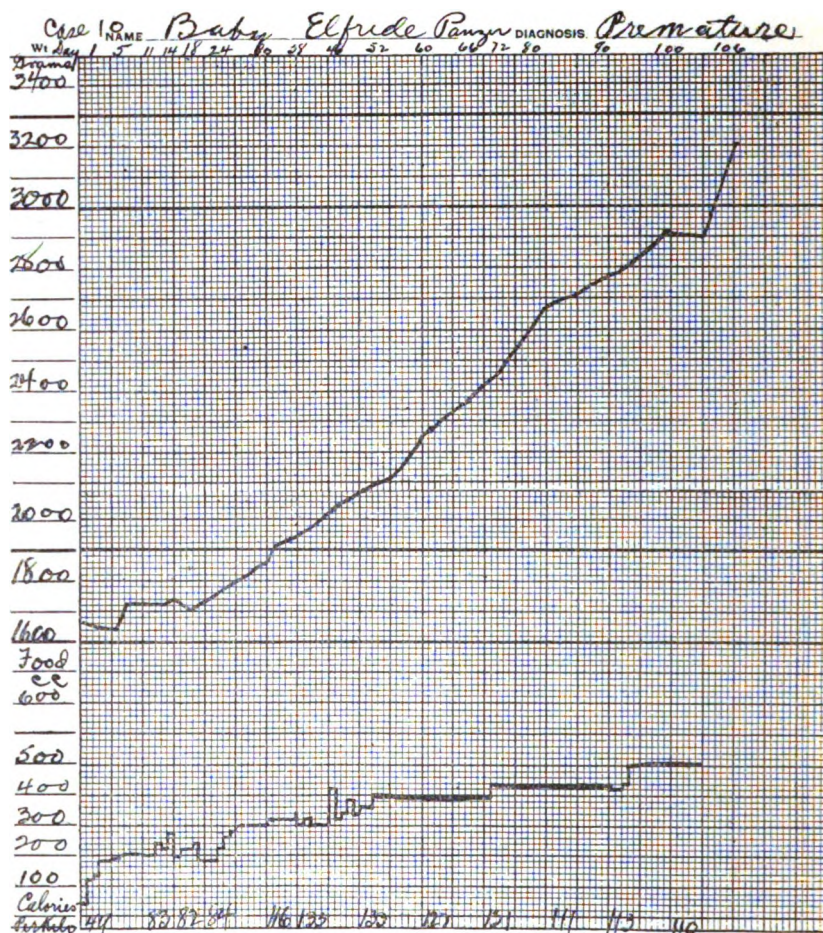


Chart 10.—Weight-Curve in Case 10

Age in Days	Weight, Gm.	Food per Day, c.c.	Calories per Kilo of Body Weight	Age in Days	Weight, Gm.	Food per Day, c.c.	Calories per Kilo of Body Weight
1	1,680	40	49	30	1,810	300	116
2	1,690	120	..	32	1,825	240	...
4	1,680	190	..	34	1,860	260	...
6	1,680	195	..	38	1,900	310	114
8	1,645	190	..	40	1,920	365	133
10	1,680	200	83	43	1,940	410	147
12	1,695	200	..	46	2,000	380	133
14	1,710	220	..	48	2,015	350	...
15*	1,720	260	..	52	2,100	400	112
16	1,720	200	82	60	2,200	400	135
18	1,700	220	..	65	2,300	400	127
20	1,710	240	..	70	2,400	450	117
21	1,740	190	84	75	2,500	450	131
24	1,740	210	..	83	2,660	450	126
26	1,745	245	..	90	2,760	450	111
28	1,765	270	..	95	2,800	440	113
				100	2,960	500	110

*First day of nursing.

At this stage artificial feeding was gradually substituted for breast milk, the gain going steadily on after a loss of 80 gm., when the breast was entirely discontinued.

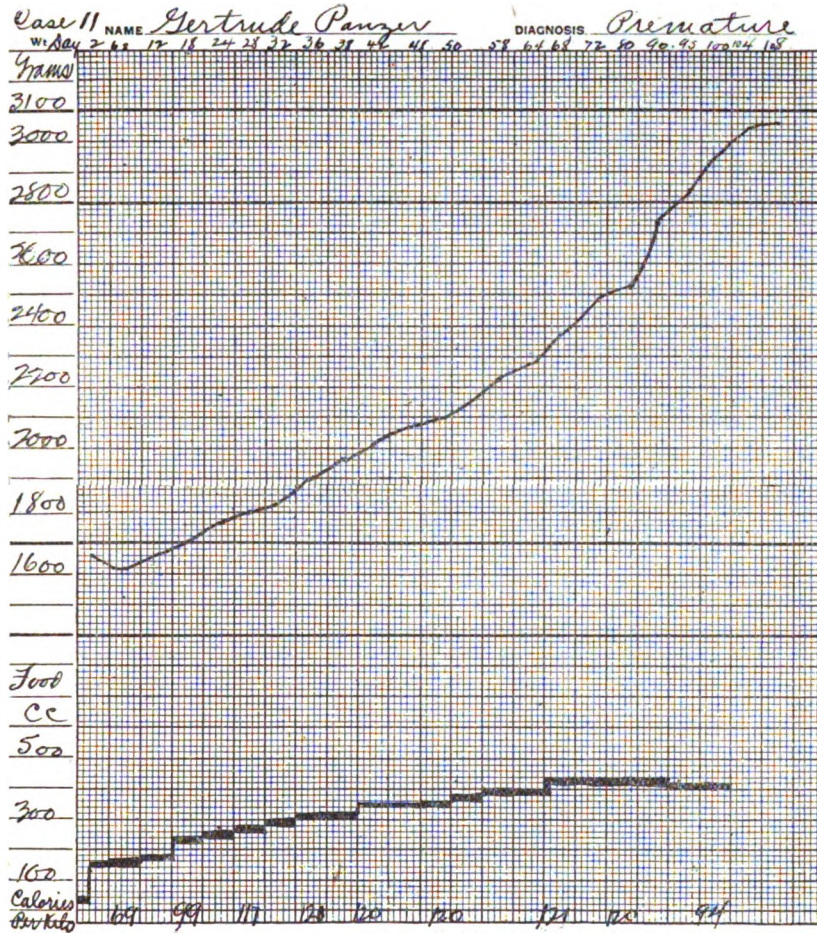


Chart 11.—Weight-Curve in Case 11

CASE 11.—Gertrude P., twin sister of Case 10. Birth weight 1,680 gm. Fed at five-hour intervals from birth.

Age in Days	Weight, Gm.	Food per Day, c.c.	Calories per Kilo of Body Weight	Age in Days	Weight, Gm.	Food per Day, c.c.	Calories per Kilo of Body Weight
1	1,680	30	..	30	1,800	300	117
2	1,660	145	..	34	1,900	315	...
4	1,690	100	..	40	1,960	345	120
6	1,635	160	..	46	2,020	340	...
8	1,620	160	69	50	2,060	360	120
10	1,690	200	82	54	2,150	400	125
14	1,690	240	..	60	2,220	400	126
16	1,695	220	99	65	2,300	400	121
18	1,700	240	..	70	2,420	440	131
20	1,720	250	...	80	2,530	440	121
24	1,760	280	103	90	2,745	420	106
26	1,790	300	...	100	2,980	400	94

At this stage artificial feeding was gradually substituted for breast milk, the gain going steadily on after a loss of 80 gm., when the breast was entirely discontinued.

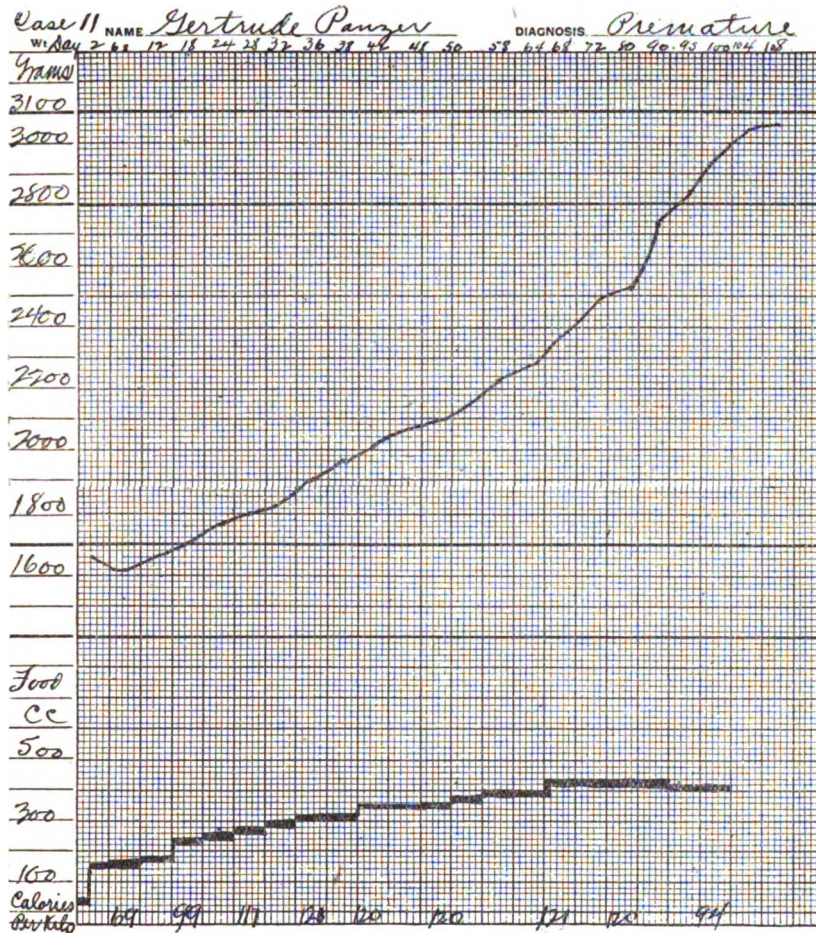


Chart 11.—Weight-Curve in Case 11

CASE 11.—Gertrude P., twin sister of Case 10. Birth weight 1,680 gm. Fed at five-hour intervals from birth.

Age in Days	Weight, Gm.	Food per Day, c.c.	Calories per Kilo of Body Weight	Age in Days	Weight, Gm.	Food per Day, c.c.	Calories per Kilo of Body Weight
1	1,680	30	..	30	1,800	300	117
2	1,660	145	..	34	1,900	315	...
4	1,690	100	..	40	1,960	345	120
6	1,635	160	..	46	2,020	340	...
8	1,620	160	69	50	2,060	360	120
10	1,690	200	82	54	2,150	400	125
14	1,690	240	..	60	2,220	400	126
16	1,695	220	99	65	2,300	400	121
18	1,700	240	..	70	2,420	440	131
20	1,720	250	...	80	2,530	440	121
24	1,760	260	103	90	2,745	420	106
26	1,790	300	...	100	2,980	400	94

As in Case 10 artificial feeding was gradually substituted with a loss of a few grams when breast feeding was entirely discontinued, followed by a steady gain

CASE 12.—Kurt S., born Jan. 11, 1909, birth weight 2,340 gm.

This child was fed albumin milk at two and a half hour intervals at first, later increased to three and then to four hour intervals. The baby was in miserable condition on admission.

Age in Days	Weight, Gm.	Food per Day, c.c.	Calories per Kilo of Body Weight	Per cent. Dextri Maltose Added	Age in Days	Weight, Gm.	Food per Day, c.c.	Calories per Kilo of Body Weight	Per cent. Dextri Maltose Added
1	2,340	290	112	1	17	2,200	500	119	..
3	2,440	400	19	2,120	500	165	..
4	2,400	400	23	2,200	500	151	..
5	2,300	400	29	2,340	500	143	..
6	2,190	400	31	2,460	500	142	..
10	2,100	400	128	2	39	2,540	600	...	4
11	2,090	480	41	2,620	600	160	..
13	2,100	500	169	3	47	2,725	600	154	..

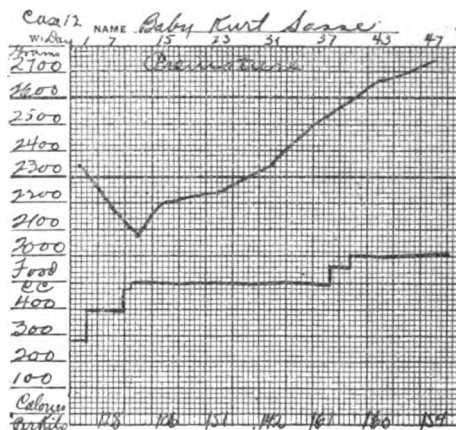


Chart 12.—Weight-Curve in Case 12

It will be noted here the greater quantity of food required and the irregularity of the weight curve when artificial food is used.

CASE 13.—George S., twin brother of Case 12, fed with the same food at two and a half hour intervals, later increased to three.

Age in Days	Weight, Gm.	Food per Day, c.c.	Calories per Kilo of Body Weight	Age in Days	Weight, Gm.	Food per Day, c.c.	Calories per Kilo of Body Weight
1*	2,540	280	77	20	2,460	500	134
3†	2,500	400	112	22	2,540	500	141
8	2,400	400	...	24	2,500	585	140
10‡	2,440	400	114	25	2,600	600	163
12	2,420	480	134	30	2,690	600	161
16	2,500	500	...	35	2,740	640	163
18	2,600	500	140				

*Albumin milk.

†1 per cent. dextri maltose added.

‡2 per cent. dextri maltose added.

Another illustration of how much more difficult artificial feeding is than feeding on the breast.

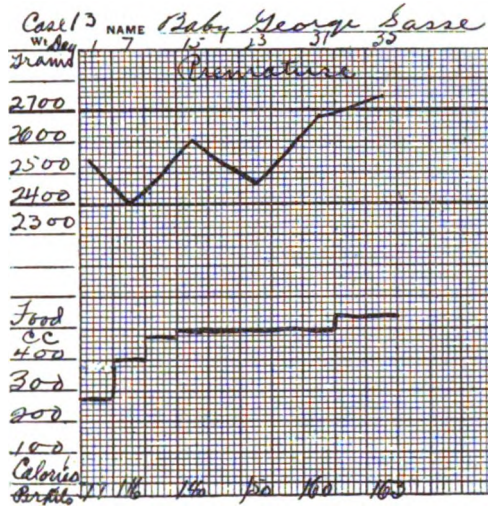


Chart 13.—Weight-Curve in Case 13

CASE 14.—Franziska S., birth weight 2,500 gm., fed every four and later every five hours on artificial food—oatmeal-water, buttermilk with varying percentages of dextri maltose cane-sugar and Liebig's malt extract, but inasmuch as we are not

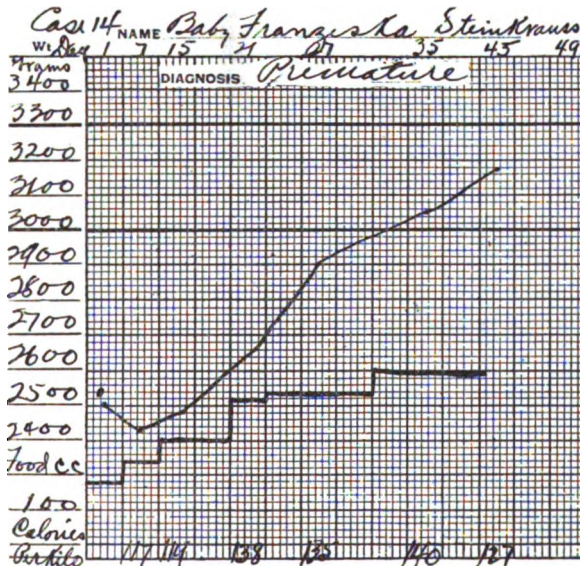


Chart 14.—Weight-Curve in Case 14

discussing the value of different artificial foods I will deal only with the quantities and caloric values.

Age in Days	Weight, Gm.	Food per Day, c.c.	Calories per Kilo of Body Weight	Age in Days	Weight, Gm.	Food per Day, c.c.	Calories per Kilo of Body Weight
1	2,500	30	..	22	2,660	525	..
2	2,500	180	..	26	2,800	540	135
4	2,480	220	79	30	2,900	600	145
6	2,500	280	78	32	3,000	600	140
8	2,460	400	113	38	3,120	600	134
12	2,480	420	119	45	3,300	600	127
18	2,580	510	138				

This case shows that with carefully regulated artificial feeding given at long intervals a continuous rapid gain is possible.

CASE 15.—Elsie S., twin sister of Case 13, fed in the same manner. Birth weight 2,140 gm.

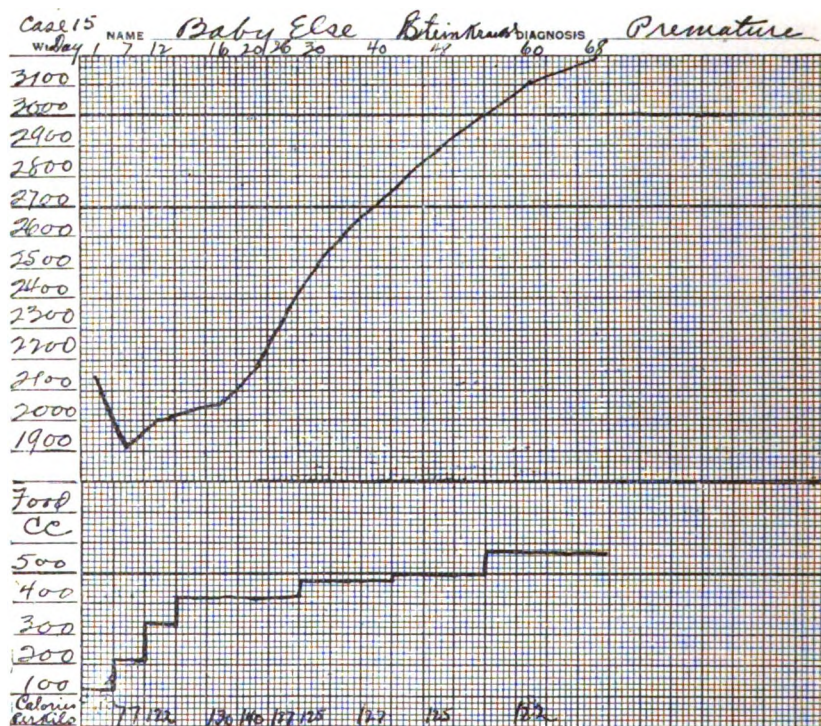


Chart 15.—Weight-Curve in Case 15

Age in Days	Weight, Gm.	Food per Day, c.c.	Calories per Kilo of Body Weight	Age in Days	Weight, Gm.	Food per Day, c.c.	Calories per Kilo of Body Weight
1	2,140	20	..	32	2,440	420	125
3	1,910	120	77	35	2,500	420	117
6	2,000	220	108	40	2,600	480	129
8	2,060	320	122	42	2,700	480	120
12	2,010	350	130	48	2,810	500	125
15	1,950	360	122	53	2,900	510	123
20	2,100	420	140	58	3,000	570	118
24	2,180	420	130	62	3,140	570	127
26	2,300	420	127				

I realize that this series is too small to permit of any positive conclusions, but the cases do show that premature babies may be successfully nourished with long interval feeding and with a minimum of digestive troubles, and in my experience with much less disturbance than with frequent feeding. The amount of care that these babies require is greatly reduced by this method of feeding. We know that the less they are handled the better the premature infant progresses. It is evident that if they are fed only every four hours they will be handled half as much, and consequently they have more time to sleep, and the long periods of sleep was one of the characteristic things about the babies of this series. The nurses have remarked about the simplicity of the care over the older method.

It may be only a coincidence, or due to the small number of cases, but not one case of this series had digestive trouble, vomiting, cyanosis or persistent green stools, except Case 1, before the long intervals were employed, and Case 7, in which we had difficulty in obtaining enough mother's milk. The vomiting in this case being due, as Budin has pointed out, to insufficient food, stopping as soon as enough food was obtained.

In searching the literature I find scant support for the long interval feeding, but what little there is, is from an eminent source. To quote from Czerny and Keller:¹

We allow the premature child no more than six meals a day (every four hours) of mother's milk, and no more than five in the case of artificial feeding. We take a stand in this respect contrary to that of almost all authors who, on account of fear of underfeeding, feed the premature baby still oftener than the mature, often hourly or half hourly. All of the reasons which we have given for feeding the mature baby at long intervals have even more weight in the case of the premature. One can determine by the scales that the quantity of nourishment which the premature baby nurses spontaneously is insufficient, and on that account loses weight; this is no reason for increasing the number of meals but, on the contrary, is reason for increasing the size of the single meal by instilling a definite amount of milk in addition to that spontaneously taken.

The weight curves of the babies in this series certainly show that a constant steady gain is possible by this method of feeding.

Inasmuch as we are limiting the discussion in this paper primarily to the feeding intervals, the question of the amount of food necessary to the proper development of the premature infant would have no place were it not that the short interval is employed through fear of under-feeding on account of the fact that the nourishment needs of the premature child are relatively larger than of the mature. The question then naturally arises as to whether it is possible for the premature child to obtain the necessarily large amount of nourishment if the long interval is employed.

1. Czerny and Keller: *Ernährung des gesunden Kindes*, p. 685.

Budin² asserts that at the tenth day of life the baby should be receiving about one-fifth or one-sixth of its body weight in food. Delestre³ substantially agrees with Budin, asserting that premature babies weighing under 1,500 gm. should receive by the tenth day, 250 gm., and over 1,500 gm. should get 350 gm.

Our Cases 2, 3 and 5 began to gain on food amounting to only one-tenth of the body weight and continued to gain on one-eighth to one-ninth, and Case 6 began to gain on one-eleventh and continued to gain on one-ninth and one-tenth. Cases 10 and 11 were receiving one-eighth when they began to gain and the progress was maintained on one-sixth to one-seventh. Cases 12, 13, 14 and 15 were fed artificially and received one-sixth, one-ninth and one-fifth, respectively. There is not a great abundance of evidence in the literature as to how much the premature infant should receive after the tenth day, but most authors recommend about one-fifth of the body weight in twenty-four hours, or 120 to 140 calories of food per kilogram of body weight.

Hess⁴ believes that the caloric needs vary inversely with the age and birth weight, the energy quotient ranging from 115 to 170 in those below 1,500 gm., and 100 to 132 in those over 1,500 gm.

Morse⁵ draws the wise conclusion that the contradictory figures of various authors as to the caloric needs of premature babies at different ages seemed to depend as much, or more, on the digestion and metabolism of the given baby, at the given age as on the amount of food, the age of the baby or any inherent differences in the individual babies.

Heubner⁶ avers that an energy quotient of less than 70 is insufficient.

As I have shown in the analysis of the individual cases, these babies can take the required amount of food without difficulty or digestive disturbance.

Case 2 took 310 c.c., or 124 calories per kilo, at the twenty-fourth day without difficulty; Case 4 took 240 c.c., an energy quotient of 75 by the tenth day; Case 5 took 205 c.c., energy quotient of 72 by the fourteenth day, and by the twenty-ninth day took 470 c.c. (energy quotient 240) and never was disturbed; Cases 10 and 11 were taking 200 c.c., and Cases 12, 13 and 14, 400 c.c., and Case 15, 350 c.c. at the tenth day, showing that the large amount of food needed can be taken without difficulty.

While these deductions by the authors of the food need are valuable, they are at best not much more than good guides as to what to attempt, for in the last analysis the weight curve and digestive ability of the individual child must be the real criterion.

2. Budin: *Manuel pratique d'allaitement*, p. 87. Paris, 1905.

3. Delestre: *Thèse de Paris*, 1901.

4. Hess: *AM. JOUR. DIS. CHILD.*, November, 1911.

5. Morse: *Am. Jour. Med. Sc.*, cxxvii, 471.

6. Heubner: *Ztschr. f. Diätet. u. physik. Therap.*, 1901, v, 13.

According to these standards our babies certainly progressed very well, for they all gained continuously and never had any digestive troubles of any kind and were far less care than if they had been fed frequently. What more could be asked?

CONCLUSIONS

1. Long interval feeding of premature infants is feasible.
2. The relatively large amount of nourishment required can be given without trouble.
3. In this series the digestive and other disturbances were less than in other cases in which the short intervals were used.
4. The weight increased as rapidly as by the other method.
5. The infants slept more and longer and were much easier to care for.
6. The best interval seems to be four hours.

I wish to acknowledge my gratitude to Drs. Adair and Schlutz for valuable aid.

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PROGRESS IN PEDIATRICS

RESPIRATORY SYSTEM

BORDEN S. VEEDER, M.D.

ST. LOUIS

RESPIRATION

Ssokolow¹ has constructed an instrument which he calls a differential pneumograph, by means of which the respiratory excursion of different parts of the chest is registered on a kymograph. Tracings taken from cases are shown and some of these are accompanied by radiographs showing the intrathoracic conditions which were present. By means of the instrument the restricted excursion of one side of the chest in case of tuberculosis of the lungs is graphically contrasted with the movement of the opposite side. Ssokolow² has also described a method of artificial respiration which he has used with success for a number of years in asphyxia of the newborn, and in other conditions requiring artificial respiration. He thinks the method is of more service and less likely to produce mechanical injury than any of the other methods in use.

By means of a specially constructed spirometer, Lederer and Vogt³ investigated the respiratory volume in infants and the effect of certain drugs on the volume. The investigations were carried on during sleep in order to avoid psychic disturbances. They found in infants that the average amount of air inspired in a single respiration is greater in sleep than when awake, but that this difference does not occur in older children. The depth of single inspirations increases from birth on. The amount of air inspired during a period of one minute (*Atmungsgrosse*) decreases during the first year of life and later remains at an almost stationary figure. The influence of alcohol was investigated, but without any very definite results being obtained. The authors think that their results indicate that alcohol has the tendency to increase the respiratory volume. In cases of chronic lung disease (bronchiectasis) the volume of air inspired was less than in normal children. They found that when the volume of the respiration increases in a normal child, the respiratory rate diminishes. In cases of chronic lung disease, on the other hand, the frequency of the respirations remains the same or even increases when the volume of air inspired is increased.

1. Ssokolow: *Jahrb. f. Kinderh.*, 1912, xxv, 265.

2. Ssokolow: *Monatschr. f. Kinderh.*, 1911, x, 457.

3. Lederer and Vogt: *Jahrb. f. Kinderh.*, 1912, xxv, 1.

Conner and Stillman⁴ studied the respiratory rhythm in meningitis by means of a Marey pneumograph. In all, 43 cases were studied which included 19 cases occurring in infants and 11 in older children. Of the 43 cases, 39 were tuberculous. They noted three types of irregularities: 1. An undulatory type, characterized by more or less rhythmical variations in the force of respirations, and in the tonicity of the respiratory muscles. This was noted at some time in the course of almost every case. 2. Biot's breathing. This was noted in 27 per cent. of the cases, but was more common in adults and in non-tuberculous cases. Biot's breathing shows a constant irregularity in the force and rhythm of the individual respirations, while periods of apnea of varying length occur at irregular intervals. Deep sighing respirations occur frequently. 3. Cheyne-Stokes respiration. This was observed in 19 (63 per cent.) of the 30 cases occurring in infants and children, and was more commonly associated with tuberculous meningitis. In infants and young children Cheyne-Stokes respiration presents certain features which distinguish it sharply from the Cheyne-Stokes respiration of adults. This, which they call the *infantile type*, they consider to be the same as the "grouped respirations" described by West. The peculiarities are described as follows: The duration of a complete cycle (respiratory period and period of apnea) is much shortened—the average time being ten seconds in contrast with the average time of one minute for a cycle in an adult. The number of respirations in each period is smaller, averaging from 4 to 5. The time of the period of apnea is relatively long and occupies one-half of the cycle, while in the adult type the respiratory period is twice the length of the period of apnea. The force and amplitude of the respiratory movements are less, and the gradual increase of amplitude followed by a gradual decrease is not so common. At times all of the respirations have practically the same amplitude in the infantile type.

THYMIC ASTHMA

During recent years the reports of a number of cases of hypertrophy of the thymus which have been treated by the x-ray have appeared in literature. Friedlander⁵ has studied the action of the x-ray on the thymus gland in litters of young rabbits, and has found that involution may be brought about in varying degrees of rapidity according to the number and frequency of exposures. Some reduction in size of the spleen occurs at the same time even when the splenic area is shut off from exposure to the rays. From his clinical and experimental studies Friedlander believes that exposure to the x-rays is a better and safer method of treatment of hypertrophied thymus than thymectomy, as the latter may produce severe metabolic disturbances.

4. Conner and Stillman: Arch. Int. Med., 1912, ix, 203.

5. Friedlander: Arch. Pediat., 1911, xxviii, 811.

In a discussion of thymic death—cases of sudden death occurring in infants or children in which an enlarged thymus is found, although no symptoms of enlargement have been present—Ssokolow⁶ takes the position that the enlarged thymus is not the cause of the death except in that it may be a sign of some underlying metabolic disturbance which is itself the cause of the death. That is, there is no such thing as thymic death without thymic asthma, although there is thymic asthma without thymic death. A number of cases are reported of dyspnea with hypertrophy of the thymus, and the author concludes that thymic asthma is a clinical entity due to the pressure of an enlarged thymus on the trachea. A rather unusual cause of enlargement of the thymus was reported by Kennedy,⁷ who found a thymus weighing 2½ ounces in a child dying of cardiac failure. Histologically the enlargement was due to an angiomatous condition of the thymus.

TRACHEOBRONCHIAL ADENOPATHY

Greult⁸ discusses the production, frequency and clinical importance of lesions of the tracheobronchial lymph-nodes. He states that enlargement is by no means always tuberculous in nature, and that marked swelling occurs in pertussis and in typhoid fever. Whether tubercular enlargement is primary or secondary is a question that is not yet definitely decided. The author thinks that even slight compression of the air passages by enlarged glands produces a respiratory murmur which is almost constantly present.

Maillet,⁹ in an interesting, although somewhat hypothetical article, discusses the acute accidents or complications which may appear in the course of tracheobronchial adenopathy. He divides these into respiratory, circulatory and digestive crises. The respiratory crises are the most common and best known and appear in two chief forms, spasm of the glottis and asthmatic attacks. The acute attacks have a sudden onset and last for an indefinite period of time. Clinically the subject of an attack is dyspneic, respirations are rapid and a stridor is present. The stridor may be inspiratory alone, or it may be accompanied by an expiratory stridor. Frequently the attacks are accompanied or followed by bronchitis and congestion, and sometimes by bronchopneumonia. Maillet considers that these acute attacks are the result of pressure of the enlarged glands on the vagus nerve or its branches. The attack may so simulate thymic asthma that it is almost impossible to distinguish the two. The dyspnea, alterations in breath sounds, and area of impaired resonance anteriorly, may be the same in both conditions. Even a radio-

6. Ssokolow: Arch. f. Kinderh., 1912, lvii, 1.

7. Kennedy: Glasgow Med. Jour., 1912, lxxii, 31.

8. Greult: Ann. de méd. et Chir. inf., 1911, xv, 497.

9. Maillet: Arch. d. méd. d. enf., 1912, xv, 193.

graph may be unable to help the diagnosis. The author states that the most important clinical sign pointing to enlarged glands rather than enlarged thymus is an area of impaired resonance posteriorly in the area over the bronchial lymph-nodes. Less commonly crises occur in which cyanosis, hemorrhage from the nose or pulmonary hemorrhage, or pulmonary edema occurs, and these attacks Maillet considers the result of vascular compression and calls circulatory accident. Certain cases of vomiting in which no distinctive signs of gastric disturbance are present, but in which the signs of enlarged bronchial glands are found on examination, the author considers as a result of the adenopathy and classifies as digestive crises.

ASTHMA

Knopf,¹⁰ in a discussion of asthma in childhood considers asthma as a symptom-complex rather than a disease *sui generis*. He bases his views on the failure to find any features peculiar to asthma and the lack of an anatomic basis for the condition. He looks on the symptom-complex as a neurosis which has its origin in a congenital weakness and hyperexcitability of the nervous system. Anxiety plays an important part in the etiology. The attacks symptomatically are a faulty coordination in the musculature of the respiratory system, so that muscles which should act as synergists act as antagonists, with the result that the effect of the strong muscular exertion is nullified. It is essential in the treatment to correct the underlying neurotic element and for this purpose it may be best to have the patient in a sanatorium. Breathing exercises accompanied by massage give better results in children than any medicine. In five cases of asthma in children, Knopf has had a symptomatic cure for over a year.

Comby¹¹ has observed 75 cases of asthma in infants and children and gives some interesting figures. The onset of the first asthmatic attack appeared 9 times in the first 6 months of life, 15 times between 6 and 12 months, 32 times between 1 and 3 years, 9 times between 3 and 6 years, and 10 times after 6 years. Of the 75 cases 43 were in boys and 32 in girls. In 21 cases there was a history of asthma in the parents of the child and in 16 cases in the grandparents. It was more common in children coming from families of the better classes, and especially from families with rheumatic or gouty tendencies. Comby looks on asthma in the infant as a manifestation of a neuro-arthritis diathesis, and it is frequently accompanied by other signs of this condition, as migraine. In 28 of the 75 cases there was a previous history of eczema. True asthma is never caused by adenoid growths nor has it any relation to tuberculosis.

10 Knopf: *Ztschr. f. Kinderh.*, 1912, ii, Ref., p. 756.

11. Comby: *Arch. d. méd. d. enf.*, 1911, xiv, 721.

BRONCHIECTASIS

Vogt¹² reports twenty-two cases of chronic respiratory disease in children in which he believes the lesion present to be bronchiectasis and discusses the condition in some detail. In these cases it is usual to find the history of a chronic bronchopneumonia or a chronic or recurrent acute bronchitis. The patients present a picture of general ill health, together with a chronic cough with expectoration. On physical examination areas are found over which râles are inconstantly present and occasionally increased respiratory sounds are heard. If there has been an old pleurisy there may be slight impairment of resonance. The picture is very similar to that of tuberculosis and Vogt believes that this is frequently erroneously diagnosed. It is best distinguished by the failure to find tubercle bacilli in the sputum on repeated examination. In some cases with dilated bronchioles, which have come to autopsy through some intercurrent disease, Vogt has found the influenza bacillus and considers this organism of importance in the etiology. In the majority of cases which follow a chronic bronchopneumonia the dilatation of the bronchi is due to a contraction of the lung with scar tissue formation or to an inflammatory destruction of the elastic and muscular tissue of the walls of the bronchi.

Fisher¹³ considers recurrent attacks of bronchitis to be the most common chronic lung disease of childhood and believes that they frequently lead to bronchiectasis. He thinks that bronchiectasis is frequently a sequel of measles, more so than is tuberculosis. He does not believe that pertussis or enlarged bronchial glands are common causes of bronchiectasis.

Buchmann¹⁴ investigated a number of cases of fetal atelectasis with secondary bronchiectasis in the area surrounding the atelectasis. Clinically these areas can only be recognized through the secondary bronchiectasis. The pleura over the atelectatic areas was thickened and showed a loss of pigment. Numerous muscle fibers were found in the interstitial tissue about the bronchiectatic cavities. No tuberculous lesions were found in the patients examined by the author.

PNEUMONIA

Numerous attempts have been made to produce pneumonia experimentally, but it has never been accomplished with any degree of success until the past year. Lamar and Meltzer,¹⁵ by means of intratracheal insufflation of pure cultures of pneumococci, were able to produce pneumonia successively in forty-two dogs. There was a mortality of 16 per cent., and in the fatal cases the lesions closely resembled those occurring

12. Vogt: *Jahrb. f. Kinderh.*, 1911, lxxiv, 627.

13. Fisher: *Clin. Jour.*, 1911-12, xxxix, 410.

14. Buchmann: *Frankfort Ztschr. f. Path.*, 1911, viii, 263.

15. Lamar and Meltzer: *Jour. Exper. Med.*, 1912, xv, 133.

in man. Clinically the non-fatal cases ran a shorter and milder course than the pneumonia occurring in man. The quantity of the culture seemed to bear a relationship to the outcome of the disease as in the fatal cases larger quantities of pneumococci were used. The authors think that the successful results were due to the obliteration of the smaller bronchi by the injected culture, which permitted the organisms to display their pathogenic activities. Wollstein and Meltzer¹⁶ continued the work, using cultures of streptococci and the influenza bacillus, and produced a lesion resembling the bronchopneumonia of man and differing materially from the lesion produced by the pneumococcus. In the experiments the animals used were not selected, and hence the authors are led to believe that the proper invasion of the organism is the determining factor in the production of a pneumonia. Furthermore, that in all probability different types of pneumonia are produced by specifically different bacteria. Whether or not the degree of virulence of the causative organisms bears a relationship to the type of pneumonia lesion produced remains for future investigation.

Hutchinson,¹⁷ in a discussion of the pneumonias of childhood, divides them into primary and secondary. He defines primary pneumonia as those cases in which the inflammation starts in the lung substances, and secondary as those in which it starts in the air passages (bronchopneumonia). Primary pneumonia may be lobar or lobular in its distribution and is practically always due to the pneumococcus. Its maximum incidence as regards age is between 1 and 2 years. The onset is usually abrupt, although often deceptive, as an attack may be ushered in by vomiting or simply drowsiness of the child. Fever and shivering may occur and convulsions are not uncommon, but a true chill is unusual. Very characteristic is the altered respiration—increase of rate frequently out of proportion to the pulse, with inversion of the respiratory rhythm (pause after inspiration). The physical signs are often absent in beginning pneumonia in children, and rarely the signs do not become manifest until the crisis is past. Impaired resonance is an important sign, and in obtaining this Hutchinson urges the value and necessity of using very light percussion. The symptoms are usually less pronounced in children than in adults, as children do not seem to suffer so much from the toxemia. Heart failure is a rare occurrence in childhood. As a rule primary pneumonia terminates by crisis on the seventh or eighth day, but it is not infrequent to have pseudo-crises. In these, however, the respiratory rate does not fall as it does in the true crises. After a crisis it is not uncommon to have an unstable temperature in children. Persistent cases may be due to protraction or there may be a spreading

16. Wollstein and Meltzer: *Jour. Exper. Med.*, 1912, xvi, 126.

17. Hutchinson: *Clin. Jour.*, 1912, xxxix, 289.

or relapsing of the primary focus of inflammation. The prognosis usually is good, and the author summarizes his treatment by saying that his cases "get really nothing which can be described as treatment at all, and I find that they do very well without it."

Niles and Meara¹⁸ report a case of lobar pneumonia in a boy of 14 years, which was due to infection with the *Micrococcus catarrhalis*. Blood cultures and cultures from a pleural exudate were sterile, but pure cultures of this organism were obtained from the sputum. Trevisanello¹⁹ obtained pure cultures of Fraenkel's diplococcus from herpetic lesions in two cases of pneumonia. Implantation of the organisms on the skin of another patient produced an herpetic eruption. The organisms were of low virulence, but the author thinks they may be capable of infecting susceptible individuals.

A case of probable antenatal pneumonia was reported by Macdonald,²⁰ the history of which was as follows: On the 17th of the month a woman at term was admitted to the hospital suffering with pneumonia. Two days later she gave birth to a female infant weighing 6 pounds. The baby was cyanosed, but cried shortly after birth. All that day the infant had difficulty in breathing and died twenty-eight days after delivery. At necropsy the upper and lower lobes of the right lung were found in a stage of red hepatization, and from the lesion cultures of pneumococci were obtained. The author thinks that from the advanced stage of the lesions found the infection must have occurred through the placental circulation before birth.

By means of a Faught sphygmomanometer, Howland and Hoobler²¹ determined the effect of cold fresh air on the blood-pressure of children with pneumonia. When children with an active pneumonia were taken from the ward and exposed to cold air on a balcony there was a rise of blood-pressure, and return to a warm, although well ventilated ward, was followed by a fall. The rise is usually noticed about a half hour after the child is put out of doors, reaches its maximum in two hours, and is maintained for a number of hours afterwards. In convalescents the change in blood-pressure was less striking and in some cases did not occur. In warm weather no effect is obtained by putting the children out of doors, and hence the authors think that the coldness of the air is the important factor, and that its action is by a reflex stimulation of the vasomotor centers through the action of the cold air on the skin and nasal mucous membrane. Whether it is advantageous from the standpoint of the circulation to raise the blood-pressure of a child with pneumonia, whose blood-pressure is already at an average point, the authors are not

18. Niles and Meara: Amer. Jour. Med. Sc., 1911, cxlii, 803.

19. Trevisanello: Centralbl. f. Bakteriologie, 1 Abt. Orig., 1911, ix, 69.

20. Macdonald: Brit. Med. Jour., 1911, ii, 1247.

21. Howland and Hoobler: AMER. JOUR. DIS. CHILD., 1912, iii, 294.

prepared to state. No bad effects were noted. The other beneficial effects of cold fresh air are not discussed in the paper.

EMPHYEMA

In an article on the diagnosis of pleuritic effusions in infancy, Miller²² draws attention to the fact that practically all pleural effusions in infancy are purulent. They are never primary and most commonly follow pneumonia. The general symptoms of a child with empyema are marked, but the physical signs are indefinite and variable. Vocal fremitus is of little value. Dulness on percussion is not always present. Bronchial breathing and râles are usually heard over an effusion. Exploratory puncture is the decisive and only sure means of diagnosing a pleural effusion. Next to this come dulness and a sense of resistance on percussion and displacement of the apex.

Zybell²³ reports 22 cases of empyema occurring in the first year of life and reviews the literature. In 14 of 20 cases examined the pneumococcus was found. Only 4 of the 22 cases were admitted to the hospital for pneumonia, but in practically all the pleural effusion was preceded or accompanied by pneumonia. He also considers exploratory puncture to be the most important and often the only useful means of diagnosis. The prognosis of empyema in infants is bad, and 15 of the 22 infants died. The cases which recovered were all among the older infants. In a discussion of the treatment Zybell is strongly in favor of aspiration or repeated puncture with a good sized cannula. He is opposed to a radical operation in infants (resection of a rib) and quotes a number of statistics to show that with resection the mortality is higher than in cases treated by aspiration or puncture. Kelly,²⁴ while in favor of drainage with children, notes that previous aspiration may be of benefit, and that in very young or very feeble infants simple incision under local anesthesia is better than resection of a rib.

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22. Miller: *Arch. Pediat.*, 1911, xxviii, 28.

23. Zybell: *Monatschr. f. Kinderh.*, 1912, Orig. xi, 93.

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